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**A
Report
on the Use of
Radioactive Materials
in
Human Subject Research
that Involved
Residents of
State-Operated Facilities
within the
Commonwealth of Massachusetts
from
1943 through 1973**

The Task Force on Human Subject Research

942/139

**A
Report
on the Use of
Radioactive Materials
in
Human Subject Research
that Involved
Residents of
State-Operated Facilities
within the
Commonwealth of Massachusetts
from
1943 through 1973**

Submitted by
the
Task Force on Human Subject Research
to
Philip Campbell, Commissioner
Commonwealth of Massachusetts
Executive Office of Health & Human Services
Department of Mental Retardation
April 1994

1775

"All people are born free and equal and have certain natural, essential and unalienable rights, among which may be reckoned the right of enjoying and defending their lives and liberties; that of acquiring, possessing and protecting property; in fine, that of seeking and obtaining their safety and happiness."

Article 1: Massachusetts Declaration of Rights

1891

It was noted by the Humane Society of Washington, D.C., that a public declaration had been made by a Swedish physician (not named) that he preferred experimenting on institutionalized children because they are "cheaper than calves."

The Humane Society, Washington, D.C.

1914

Institutions were found to be the perfect place to conduct research, because the supervised and standardized conditions came as close as possible "to conditions which are insisted on in considering the course of experimental infection among laboratory animals, but which can rarely be controlled in a study of infection of man."

Alfred F. Hess, Medical Director, Hebrew Infant Asylum

1964

"Considering the nature of the population from another perspective also presents its pros and cons for research. Traditionally institutions have been assigned the deviant, the troublesome, and the discarded individuals of society. Their services have been directed toward relieving the community of its problem population and toward modifying the patients' or residents' capacity to function acceptably within the community."

Joseph J. Parnicky, Superintendent, Bordentown, N.J.

1972

"What must be recognized is the enormous ambivalence toward the sick reflected in conflicting wishes to exculpate and to blame, to sanction and not to sanction, to treat and to mistreat, to protect and to destroy."

Jay Katz, *Experimentation with Human Beings*

1976

"Mentally retarded individuals are always among the first to have their human rights denied, the first to be experimented upon, to be placed in institutions, to be sterilized, to be allowed to wither, and even, to be destroyed."

Eunice Kennedy Shriver, Joseph P. Kennedy Jr. Foundation

ACKNOWLEDGEMENTS

A project of this size and intensity can only be accomplished with the support and cooperation of many individuals, staff and volunteers.

On behalf of the Task Force membership and the Advisory Group, we wish to thank the following people:

- Tom Philbin, John Abbotts and David Moulton of Congressman Markey's office
- Vann Dunne and Jessica Riviere of Senator Kennedy's office
- Mary Barnes, Editor
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- Helen Samuel, Librarian/Archivist
- Louisa Orr, Executive Assistant
- Anne Parker, Shriver Clinical
- Susan Kilgore & Mark Leicester
- Helen Hickey
- Penny Ford Carlton and Susan Ford, MGH
- Donna Lutz
- Carol Cerf
- Bruce Gale

■ Fernald Staff:

Paul Duhamel, Bonnie Stecher, Paul Procaccini, Debbie Merrullo, Rick Fraser, Dorothy Neri, Joe Foley, Karen Liazos, Joan Rickets, Paula Potvin, Linda Gershman, Lisa Bradley, Peter Brand, Janine Dedon, Richard Dutton, Salwa Esa, James Heithmar, Maria Lazzaro, Patricia Mascelluti, David Maxfield, Judith Rheame, Stephen Rogers, Kay Schodak, Gail Wangler, Moe O'Connel, Joe Almeida.

■ Wrentham Staff:

Nick D'Alusio (Facility Director), Linda McCarthy and the Consumer Resources Department Staff, Paula Potvin and Linda Gershman of Social Services

- Staff at each of the other DMR facilities including: Monson Developmental Center, Hogan Regional Center, Dever State School, Glavin Regional Center, Templeton Developmental Center

■ DMR Central Office

Joanne Carney (Administrative Assistant to Deputy Commissioner Misilo) and Berni Davis (Administrative Assistant to Commissioner Campbell)

- And other individuals too numerous to mention

- Frederick Misilo, Task Force Chairperson
- Peter O'Meara, Task Force Manager
- Doe West, Project Coordinator



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160 North Washington Street
Boston, MA 02114

Philip Campbell
Commissioner

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April 15, 1994

To Whom It May Concern:

On December 26, 1993 the Boston Globe reported the discovery of information regarding the use of former residents of the Fernald State School as human subjects for research involving radioactive substances during the 1940's and 50's. The shock and horror of that discovery made news, literally around the world. I shared the public's disbelief that some of the most vulnerable individuals in our society were deliberately exposed to harmful substances without their consent or ability to understand the risks involved.

The Department of Mental Retardation (DMR) is the agency of state government charged with the responsibility to support and protect individuals with mental retardation. As Commissioner of DMR, I felt it was critically important to investigate those reports and fully disclose any research activity at any DMR facility that involved the use of radioactive substances. To accomplish such an immense task in a responsive manner, I appointed a task force of interested individuals who would maintain the best interest of the people involved and work diligently to discover the truth. I issued a charge which challenged the task force with an urgent time frame, knowing that it would be very difficult to accomplish. However, for the sake of those individuals who believed they may have been involved, the importance of a prompt disclosure could not be underestimated.

The individuals who agreed to accept the challenge and serve on the task force deserve wide recognition for their dedicated service. They are parents, former residents, advocates, doctors, lawyers, clergy, legislators and educators. Their common goal was to seek the truth no matter what. Since January, the task force and its sub-committees have met at least weekly. They have become experts in the history of the type of research that was occurring in that day.

I particularly wish to acknowledge and thank the parents for their unwavering focus on the well being of individuals with mental retardation, and those courageous former residents who shared their insights into institutional life of that day.

Letter from Commissioner Campbell
April 15, 1994
Page 2

I also wish to acknowledge and thank those scientists, medical personnel, and nationally known experts in matters of radiation and epidemiology who have assisted the task force members to better understand technical and scientific information.

In addition recognition goes to Deputy Commissioner Fred Misilo who agreed to chair the task force, to Peter O'Meara, Facility Director at Fernald who provided the management expertise, and to the Rev. Doe West, who was hired by the Task Force to serve as the official coordinator of the task force activities. Without their expertise and dedication this report would not have been completed.

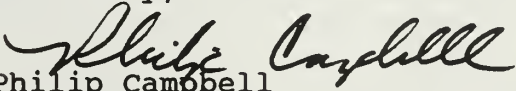
Finally, this disclosure will not be complete if it simply remains a study of history. Instead, the lessons to be learned from the life experiences of those individuals 3, 4, or 5 decades ago must be brought forth for the protection of the rights and dignity of children and adults with mental retardation today and for 3 or 4 or 5 decades yet to come.

In response to someone who asked, "Could the same thing happen today?" I offered the comment, "If you think it can't, then it probably can." The need for diligence and safeguarding vulnerable populations is a task all must accept each and every day.

I am grateful to the Task Force for their recommendations and will ensure that all necessary protections are acted upon in a timely manner.

Thank you all for a job well done.

Sincerely,


Philip Campbell
Commissioner

EDWARD M. KENNEDY MASSACHUSETTS, CHAIRMAN

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COMMITTEE ON LABOR AND
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WASHINGTON, DC 20510-6300

April 12, 1994

Frederick M. Misilo, Jr. Esq.
Chairperson
Task Force to Review Human Subjects Research
Massachusetts Department of Mental Retardation
Post Office Box 9108
Belmont, Massachusetts 02178

Dear Chairperson Misilo:

I am pleased to offer comments on the preliminary report of Task Force to Review Human Subjects Research. It is heartening to see the vigor with which the Task Force has pursued its investigation of radiation experiments on children challenged Massachusetts citizens.

As you know in 1973 I chaired a series of hearings in the Subcommittee on Health entitled the "Quality of Health Care - Human Experimentation." These landmark hearings brought to light serious violations of subjects rights as exemplified in the Tuskegee Syphilis Study, prison research, and the involuntary sterilization of the Relf sisters.

I sponsored the National Research Act in 1974 which established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The National Commission was charged with reviewing the policies protecting biomedical and behavioral research subjects and making recommendations to improve those policies. The Commission also issued recommendations for the protection of vulnerable populations, which were adopted with the exception of those protecting the mentally infirmed.

The Subcommittee on Health which I chaired, focused on the use of hallucinogenic drugs during hearings in 1975. We learned that LSD was administered by the CIA to individuals without their knowledge or consent, and resulted in a subject's suicide in one instance.

I sponsored legislation in 1978 which established the President's Commission for the Study of Ethical Problems in Medicine and Biomedical Research. My committee recognized the need for a President's Commission when we discovered the broad range of federal agencies funding biomedical and behavioral research which violated subjects' rights.



In 1983 the President's Commission recommended that Congressional Committees with oversight responsibility for biomedical and behavioral research monitor the response of administrative agencies to the Commission's recommendations on the protection of human subjects. The Commission also asked for appropriate continued oversight of local institutional review boards.


During the hearings at the Fernald School on January 13, 1994, we learned that: (1) The Fernald radiation studies were not ethically justified because they involved the use of a vulnerable population as a means to a researcher's end; and (2) Current federal regulations are insufficient to protect the rights and welfare of children and the institutionalized mentally challenged.

At the hearing we heard a call for creating an Ethics Advisory Board within the Department of Health and Human Services to provide oversight of human subject protection for research sponsored by all Federal agencies. Lastly, our attention was once again directed to implementing the 1978 recommendations for regulations on the institutionalized mentally disabled.

Currently I am drafting legislation with Mr. Markey to establish the National Commission on Biomedical ethics for the purpose of determining the scope and effectiveness of current laws to protect human subjects in biomedical and behavioral research. The Commission will direct its attention to human subjects identified as members of a vulnerable population.

I appreciate working with you on this important issue. Together we will uncover the full extent of the problem and assure this will not occur again.

Sincerely,


Edward M. Kennedy

COMMITTEES
ENERGY AND COMMERCE
CHAIRMAN
SUBCOMMITTEE ON
TELECOMMUNICATIONS AND
FINANCE
NATURAL RESOURCES
COMMISSION ON SECURITY AND
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March 4, 1994

Frederick M. Misilo, Jr., Esq.
Chairperson

The Task Force to Review Human Subject Research
Massachusetts Department of Mental Retardation
Post Office Box 9108
Belmont, Massachusetts 02178

Dear Chairperson Misilo:

It has been my privilege to be involved with the Task Force, and I am honored by your request for my comments on the occasion of the Task Force report. I am pleased to inform you that the response of officials and institutions in Massachusetts to the experiments at the Fernald School stands in stark contrast to the past response at the federal level in regard to experiments with ionizing radiation and human subjects. While it has taken years to prompt an adequate response at the federal level, the response in Massachusetts was vigorous from the outset, with the goals of full disclosure and rectification of past events.

I wish to commend the members of the Task Force, and to especially acknowledge your leadership as Chairperson. I take special note of the untiring efforts of those whose work supported the Task Force, particularly Project Manager Peter O'Meara and Project Coordinator Doe West. I also appreciate the indulgence of yourself and the other members of the Task Force in allowing members of my staff to attend meetings in my absence.

As you know, in October 1986, I released a staff report of the House Subcommittee on Energy Conservation and Power, which described experiments with human subjects and ionizing radiation that provided little or no medical benefit to those exposed. This report was based on documents requested from the Department of Energy, related to experiments funded by its predecessor agencies. The staff report recommended medical follow-up of the subjects of these experiments, and recommended that experiments of the type described, which apparently ended in the early 1970s, never be conducted again.

An Appendix to the 1986 report described current federal regulations on human experimentation, including four general principles:



March 4, 1994

- Risks to subjects should be minimized;
- Risks to subjects should be reasonable in relation to anticipated benefits, and the importance of the knowledge that may reasonably be expected to result;
- Subjects should be selected in an equitable manner; and
- Informed consent shall be sought from each prospective subject or authorized representative. Informed consent includes a clear description of the risks and benefits of the experimental procedure.

Additional restrictions are in effect for experiments with children, and such experiments generally require a benefit for the subject or a benefit for the health of children generally.

The Subcommittee staff report was essentially ignored by the Reagan administration, and it was left to gather dust on a shelf until Secretary of Energy Hazel O'Leary accepted its findings late in 1993. Secretary O'Leary and the Clinton administration, through its Human Radiation Interagency Working Group, are committed to full disclosure of experiments with ionizing radiation and human subjects, while protecting the privacy of subjects and their families, and to medical follow-up where it is feasible and indicated. Although it has taken a long time for action at the federal level, I have been gratified by the leadership of the Clinton administration on this issue.

Late in 1993, information was released on the Fernald School experiments, where schoolboys were fed radioactive iron or calcium in their breakfast meals in the 1940s and 1950s. These experiments violated at least two of the present standards for using human subjects: The children at the school represented a segment of society that deserved protection, not exploitation; and their parents were deceived about the nature of the experiments when they gave their consent for participation (details of these and other experiments are contained in the Task Force report).

In contrast to the experience at the federal level, officials of the Massachusetts Department of Mental Retardation from the outset registered profound shock and dismay over the experiments. The DMR has shown no interest in defending mistakes committed in the past. The formation of the Task Force and the investigation by its staff have been designed to provide full disclosure of the extent of human experimentation with ionizing radiation at all DMR facilities.

I have also been impressed with the response of Massachusetts academic institutions, whose affiliated scientists conducted the experiments of the 1940s, 50s, and 60s. Dr. Charles Vest, present president of MIT, acknowledged that while doses at the Fernald School may have been relatively low, he was "sorry" for the experiments, because of the children



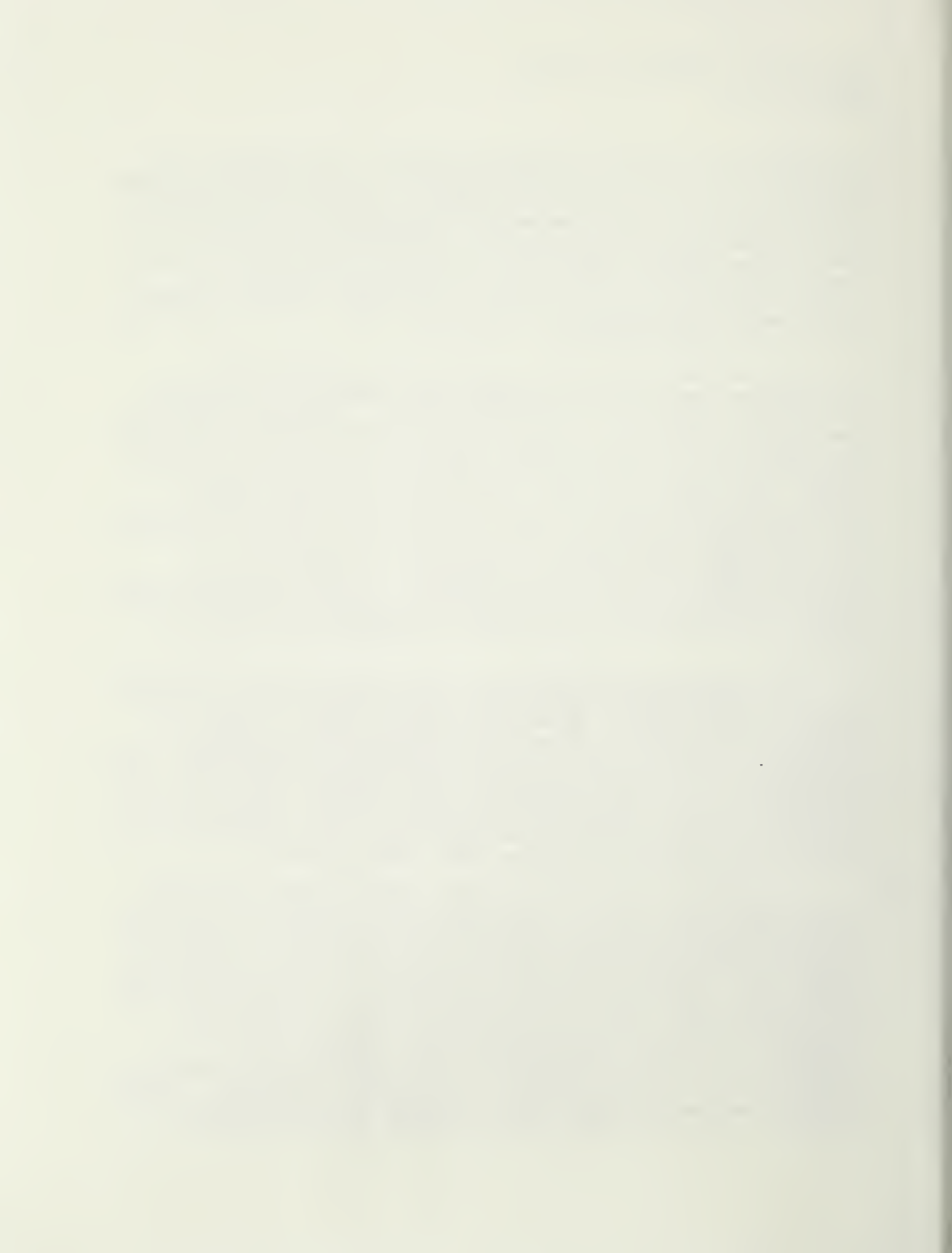
March 4, 1994

selected and the lack of informed consent. MIT explained that President Vest issued his statement because "it seemed the decent thing to do," and I applaud his decency. Likewise, the efforts of present officials and scientists at Harvard University brought to the attention of the Task Force experiments in the 1960s at the Wrentham School, where tiny children were fed non-radioactive iodide and radioactive iodine-131, to test a possible "countermeasure" to fallout from atomic bombs. Present leaders of academic institutions have been interested in full disclosure, not in defending mistakes of the past.

The revelation of these experiments at Massachusetts institutions has raised my concern over whether the full extent of testing nationally has been identified. The experiments at the Fernald School were funded in part by the National Institutes of Health and the Atomic Energy Commission, and should have been reported to my Subcommittee in response to its requests in the 1980s. The scientific paper reporting the Wrentham School experiments noted that the test subjects were chosen "because it was desirable to secure children living under constant conditions of environment, diet, and iodide uptake," and similar considerations contributed to selection of students at the Fernald School as experimental subjects. These revelations cause concern about whether institutionalized populations presented too great a temptation for experimental investigators across the country.

Accordingly, I have written to Secretary of Health and Human Services Donna Shalala, whose department is reviewing its files as part of the federal Interagency Working Group. I have requested that in its review, her Department give heightened attention to experiments on the developmentally challenged. The experiments at the Wrentham School were funded by the U.S. Public Health Service, Division of Radiological Health, and I have also requested special attention to the files of that office, to determine if other questionable experiments were conducted in the name of understanding exposures from atomic fallout.

I recognize that because of the limits of time, the Task Force report is focused on experiments with ionizing radiation. I also recognize and commend your determination in the future to examine exposures to other agents at DMR facilities. The Task Force efforts thus represent a prototype that can be replicated across the country in at least two regards: Firstly, this is to my knowledge the first systematic governmental investigation of experiments with ionizing radiation and institutionalized subjects. Secondly, the DMR has recognized that it is appropriate to investigate experimental exposures to dangerous chemical and biological agents in addition to radiation. I have already recommended expanding the efforts at the federal level to identify experiments with such additional hazardous agents.



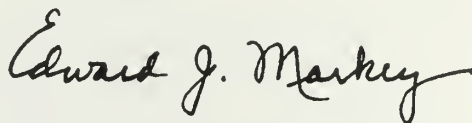
Frederick M. Misilo, Jr., Esq.

Page 4

March 4, 1994

Once again, I commend your leadership, and I appreciate the opportunity to be associated with this admirable effort. I offer whatever assistance would be appropriate in implementing the recommendations of the Task Force, and I would welcome the chance to continue assisting your investigations at the DMR.

Sincerely,

A handwritten signature in cursive script that reads "Edward J. Markey". The signature is written in dark ink and is positioned above the printed name and title.

Edward J. Markey
Member of Congress

The Task Force to Review Human Subject Research

Massachusetts Department of Mental Retardation

Task Force Members:

Dr. Marylou Buyse
Dr. Allen Crocker
Prof. Gunnar Dybwad
Charles Dyer
Dr. Anne Howard
Richard Krant
Austin LaRoque
Doris Manson
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Virginia Tisei, Esq.
David White-Lief, Esq.

Frederick M. Misilo, Jr., Esq.
Chairperson

Peter H. O'Meara
Project Manager

Doe West
Project Coordinator

April 29, 1994

Philip Campbell
Commissioner
Department of Mental Retardation
160 North Washington Street
Boston, Massachusetts 02114

Dear Commissioner Campbell:

I am pleased to present the report of the Human Subject Task Force to you. This report contains a set of findings, recommendations and an in-depth description of the series of research activities which utilized radioactive material in D.M.R. facilities from the late 1940's to the early 1960's.

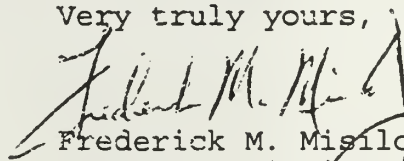
I would like to acknowledge the work and dedication of Peter O'Meara who served as the Project Manager and Doe West who served as Project Coordinator for the task force. Ms. West, who functioned in her role on a full-time basis, really deserves much of the credit for coordinating, managing and keeping the day-to-day activities of the task force on track.

I would also like to acknowledge and thank the task force members who so graciously gave of their time and support to this worthy endeavor. Their contributions to the deliberations of the task force and to the development of the final report are enormous.

I would also like to personally thank you for the support and confidence you showed in me by providing me with the opportunity to chair this task force. I hope my contributions and the work of the task force have lived up to your expectations.

It has been my privilege and honor to serve the Department of Mental Retardation on this task force.

Very truly yours,


Frederick M. Misilo, Jr.
Deputy Commissioner and
Chair, Task Force on Human
Subject Research

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The Commissioner's Charge to the Task Force on Human Subject Research

The original charge, written on December 29, 1993, stated that the Task Force on Human Subject Research was established to review and report on any and all research that utilized radioactive or other potentially harmful materials involving human subjects who resided in facilities operated by the Commonwealth of Massachusetts for persons with mental retardation, with a report due to the Commissioner by March 31, 1994.

Within the first 60 days of research and review of archival materials, the Task Force informed the Commissioner that the original charge was too broad to be accomplished within the time frame. The Task Force requested that its reporting be limited to only research that utilized radioactive materials. To continue the archival review for "other potentially harmful materials" would not be feasible in this initial review. The Task Force felt strongly that the research studies utilizing radioactive materials should be a top priority.

Furthermore, due to the establishment of federal laws pertaining to the protection of human subjects by way of institutional review boards (IRBs) in 1973, the boundary of the review was requested to end at this year. The beginning boundary was set at 1943 due to the finding of archival materials (noted in this report) that indicated the Iron study which utilized radioactive tracers was the first study done with researchers from outside Fernald.

A new charge was issued on March 22, 1994, to include these new boundaries and to set a new due date for the report to be submitted to the Commissioner by April 15, 1994.

The original and revised charges follow.



Philip Campbell
Commissioner

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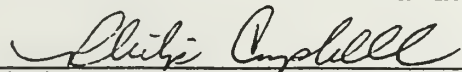
**TASK FORCE TO REVIEW HUMAN SUBJECT RESEARCH
A RE-CHARGE OF INTENT**

There is hereby established a task force to review and report on any and all research projects which utilize radioactive materials involving human subjects within the facilities for the mentally retarded operated by the Commonwealth of Massachusetts between the years 1943 and 1973, said review is to commence immediately. The task force shall report to the Office of Commissioner on or before April 15, 1994 its findings with a written report in such form as the task force members deem appropriate.

This re-charge is being enacted to accommodate the request of the members of the task force to target the scope of this initial review to address the studies utilizing radioactive materials. Further investigation into any and all studies that utilized other potentially harmful materials, as well as the addition of potentially harmful behavioral studies, shall be done as a next step of review by the Office of the Commissioner at a later date to be identified upon the acceptance of the initial report from this task force.

The task force shall be comprised of such individuals with appropriate background, training, and interest as the Commissioner shall determine appropriate. There shall be a chairperson of the task force who shall be the Deputy Commissioner, Frederick M. Misilo, Jr. The task force members shall serve at the pleasure of the Commissioner. The task force shall meet on a regular basis and shall make its major progress report to the Commissioner in writing.

Re-established this 22nd day of March, 1994


Philip Campbell, Commissioner
Department of Mental Retardation
Boston, Massachusetts



The Commonwealth of Massachusetts
Executive Office of Health & Human Services
Department of Mental Retardation
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TASK FORCE TO REVIEW HUMAN SUBJECT RESEARCH

There is hereby established a task force to review and report on any and all research projects which utilized radioactive and other potentially harmful material involving human subjects within the facilities for the mentally retarded operated by the Commonwealth of Massachusetts, said review is to commence immediately. The task force shall report to the Office of Commissioner on or before March 31, 1994 its findings with a written report in such form as the task force members deem appropriate.

This task force is being established due to the recent release of documents by the U.S. Department of Energy. These documents reveal that individuals with mental retardation were previously used by researchers in experiments involving the radioactive materials. The task force shall review and analyze all such research. It shall also attempt to identify each and every resident who participated in such research. It shall also attempt through the Department of Mental Retardation to locate all such individuals who shall be provided with information concerning the research and, particularly, the use of radioactive or other potentially harmful material. To the extent that individuals are identified who have since died from the time of the experiments, the task force shall attempt to obtain records concerning the cause of death of such former residents.

The task force shall be comprised of such individuals with appropriate background, training, and interest as the Commissioner shall determine appropriate. There shall be a chairperson of the task force who shall be The Deputy Commissioner, Frederick M. Misilo, Jr. The task force members shall serve at the pleasure of the Commissioner. The task force shall meet on a regular basis and shall make its final report to the Commissioner in writing.

Established this 29th day of December,
1993


Philip Campbell, Commissioner
Department of Mental Retardation
Boston, Massachusetts



I. Introduction

This report contains a full disclosure of the data made available to the Task Force on all identified studies utilizing radioactive materials involving human subjects who resided in facilities operated by the Commonwealth of Massachusetts for persons with mental retardation between the years 1943-1973. It is possible that studies were done for which no public records exist or exist in a place or manner not identified during this phase of the research and review. The Task Force used a vast number of information sources and consulted multiple experts in related medical, social science, and legal fields to provide as comprehensive a review as possible.

Throughout the past four decades, there have been numerous accounts documenting the experiences of persons who have been used as subjects in experiments involving radiation. A well-publicized staff report for the House Subcommittee on Energy Conservation and Power, presented by Massachusetts Congressman Edward J. Markey in 1986, described experiments with human subjects who had received ionizing radiation that provided little or no medical benefit to those exposed. While there was some public concern raised at the time, there was no administrative follow-up taken and no further public access to the data provided.

Please Take Note

Throughout this report it will be stated that many of the people who became residents of the Walter E. Fernald School, from its opening in 1848 right through the 1950s, were not admitted with a diagnosis of mental retardation. Societal and cultural norms of the day permitted persons to be admitted to state-operated institutions for a number of reasons. All were labeled mentally retarded just by virtue of having lived within the facility. The Task Force asks that the general public and members of the press take special note that these labels are grossly inaccurate, misleading, and simply not true.

In the spring of 1993, President Bill Clinton directed federal agencies to implement a post-Cold War declassification process that would allow citizens to gain access to archival records that had previously been denied to them. The Department of Energy initiated a massive release of documents for public inspection beginning in the summer of 1993. Subsequently, private citizens, advocacy groups, and the press began to review these declassified records and make public many previously unknown, or little-known experiments and research studies that had used radioactive materials throughout the United States.

In November 1993, the *Albuquerque Tribune* of New Mexico printed a series of articles by Eileen Welsome that detailed research involving the injection of plutonium into human subjects dating back to the 1940s. The reporting of these events was a catalyst for the establishment, by President Clinton, of the President's Advisory Committee on Human Radiation Studies and its Human Radiation Interagency Working Group.

On December 26, 1993, the *Boston Globe* published an article written by Scott Allen in which he identified the Walter E. Fernald School as one of the institutions in Massachusetts where radioactive material was administered to residents by researchers from the Massachusetts Institute of Technology (MIT). It was reported that young male residents of Fernald, who were members of a "Science Club," were used as subjects in nutritional studies using radioactive materials in the 1940s and 1950s.

Out of concern for the nature of the facts revealed in the *Globe* article, the identified institutions made public statements allowing that current staff was unaware of these studies and committing to work in an open and cooperative manner to respond to the need for a full and accurate public reporting.

On December 29, 1993, Philip Campbell, Commissioner of the Department of Mental Retardation (DMR), created the *Task Force on Human Subject Research* to design and conduct a comprehensive review process to secure all known facts on such studies within facilities operated by the Commonwealth.

On January 13, 1994, the Senate Committee on Labor and Human Resources held a public hearing on the grounds of Fernald that was co-chaired by Senator Edward M. Kennedy and Congressman Edward J. Markey. Among those testifying that day were a number of persons who would serve on the Task Force. Austin LaRocque and Charles Dyer testified as former "Science Club" members; Dr. J. David Litster, Vice President and Dean of Research at MIT and one of the experts whose opinions were sought on the medical risk calculation, gave scientific interpretation of the Iron and Calcium studies based on the published literature; and Frederick M. Misilo, Jr., Deputy Commissioner of the Department of Mental Retardation, testified as the Chairperson of the Task Force on Human Subject Research.

Misilo reflected deep concern on behalf of all interested parties when he stated: *"The research which involved residents as the members of a Science Club over forty years ago clearly did not obtain the informed consent of those research participants. These tests serve as a dark reminder of the vulnerability of institutionalized persons with diminished capacity to be exploited, oftentimes in name of some greater good."*

This report is divided into six major information sections:

- **The Task Force:** An overview of the specific work, policies, and procedures of the Task Force.
- **What Happened?:** A review of the radioactive tracer studies identified to date; the number of subjects involved; the radioisotope tracers used; and the dose of exposure involved.
- **Archival Record Chronology:** A comprehensive chronology of events and facts leading up to and encompassing the Iron and Calcium tracer studies conducted at Fernald. These archival records address issues such as the knowledge of the day concerning the use of radioisotopes, the rationale for and selection of Fernald as the site for the studies, correspondence with state and federal administrative agencies, and outreach to parents/guardians for permission for the subjects to participate in the research studies. By reproducing these documents in their entirety, the Task Force seeks to fulfill its mission of "full disclosure of all the facts found" in a very real and tangible manner.

- **How Could It Have Happened?:** An examination of the environment and circumstances that allowed these research studies to occur, including background on guardianship and state wards and the development of informed consent. Included in this section are first-person narratives written by former residents or parents/family members of residents of Fernald at that time.
- **Could This Happen Today?;** An examination of the current federal laws and DMR regulations that address protection in biomedical research and the significant role that the advocacy movement plays in the development of and ongoing oversight for such protective standards.
- **Findings & Recommendations:** A set of findings and recommendations that address procedural safeguards, policy revisions aimed at creating or increasing safeguards for vulnerable populations, and areas that require follow-up action.

The Task Force strongly emphasizes that those responsible for the care of persons residing in institutions or supervised placements cannot rest on these laws, regulations, or further recommendations made by this Task Force alone. The operation of these safeguards, and effectiveness of social policies meant to offer such protection must be regularly reviewed and reassessed.

In the words of the Department of Mental Retardation's Commissioner Philip Campbell, *"If you think these kinds of experiments can't happen again, then they probably will."*



The Task Force

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Chairperson

Dr. Mary Louise Buyse
Medical Director, Fernald School

Doris Manson
Parent & Advocate

Dr. Allen Crocker
Governor's Commission on MR

Rep. Edward J. Markey
U.S. House of Representatives

Dr. Gunnar Dybwad
Professor Emeritus, Brandeis

George Mavridis
Family Member & Advocate

Charles Dyer
Former member, The Science Club

The Rev. Richard Robison
Parent & Advocate

Dr. Anne Howard
DMR Statewide Advisory Committee

Virginia Tisei, Esq.
Family Member & Advocate

Richard Krant
Parent & Advocate

The Rev. Doe West
Advocate & Project Coordinator

Austin LaRocque
Former member, The Science Club

David White-Lief, Esq.
Chair, Human Rights Committee

On December 26, 1993, a *Boston Globe* article disclosed that studies using radioactive materials had been conducted at the Fernald School in the 1940s and 1950s. That same day Fernald officials, in concert with Commissioner Philip Campbell, met to identify advocates and professionals to serve on a task force that would accept and carry out the work involved to meet the stated charge.

By January 3, 1994, planning sessions were held to develop policies and procedures for review purposes. Representatives from Harvard University and the Massachusetts Institute of Technology (MIT) volunteered to assist in whatever manner deemed appropriate by the Task Force. A Task Force member, Rev. Doe West, was asked to serve as full-time Project Coordinator.

The Task Force consisted of two individuals who were themselves members of the Science Club, parents and siblings of former and current residents, lawyers, clergy, advocates, educators, physicians, and administrators. An Advisory Committee was established by the Project Coordinator to create a working group of over twenty persons whose fields of expertise included radiation, epidemiology, bioethics, the social sciences, and medical sciences. Concerned members of the Fernald staff were also asked to serve on the Advisory Committee. The

membership of the Task Force and Advisory Committee is listed in annotated form in Appendix A of this report.

An "800" telephone line (with TTY capability for those not able to use a traditional voice telephone) was established to enable individuals to call in and either provide or request information. In the first two months, over 400 calls and letters were received.

At Fernald, a full archival record review was begun that focused initially on the permanent files of those former and present residents who had lived at Fernald during the 1940s and 1950s. The review also involved any individual who was identified in an archival record, who called Fernald's "800" hotline, or who wrote a letter requesting such a review on his/her own record or on behalf of someone who lived on the grounds in that time period. About 600 records have been reviewed as of the writing of this report. It should be noted that the client/medical records are stored on site for current residents and in the state archives in Dorchester, Massachusetts, for former residents.

The Task Force went on to review the Fernald Library's archival materials, as well as personnel and administrative records found from this era. These 30- to 50-year-old records often crumbled as they were handled due to their age and condition; the data was often in primitive form or in faded handwriting.

The records lacked any standardized or obviously relevant headings. Consequently, it was necessary to conduct a very extensive review of any record or ledger found from the time period. Many records were clearly related to issues the Task Force had identified for review, but others were found in what would at first glance appear to be unrelated files. After a few such seemingly unrelated files were found to contain relevant facts, it was decided that the review had to entail a page-by-page review of literally thousands of pages of information by the Project Coordinator and supporting persons at associated archival sites.

The Project Coordinator met with state, federal, university, and hospital librarians and archivists to assure a uniform search methodology and direction that would avoid duplication of effort. Any time a record relating to the tracer studies was found that referenced another organization or institution, it was immediately shared with that organization or institution and a joint follow-up search for related documents was performed.

Key records were identified through the following means:

- Searches of published scientific literature;
- Specific literature reviews of the published works of each researcher identified in the studies;
- Copies of old annual, trustee, and departmental reports;
- A systematic search of administrative and archival files from that era found in libraries, cellars, and attics;
- Correspondence files of all administrators and medical staff; and
- Personal papers donated to university libraries with original notes and reports from the researchers.

Significantly, no original reports or specific official records on the tracer studies were found in any of the client records. On rare occasion there was a copy of a permission letter or a vague reference to outside activities discovered in routine staff notes. On a very rare occasion an indirect reference would serve as a clue that could lead to relevant information or identification; for example, a distinctive type of blood test that was known to be used in a study with no indication of illness or infirmity stay. Even more scarce were copies of letters or staff notes that clearly or obviously referred to a resident participating in a special research study or treatment. Such overt references were significantly infrequent in comparison with the number of records reviewed. Even after positive identification was made of the subjects, a second review of their records still yielded no clues to the research studies. Given these hurdles, how was the positive identification of the subjects made?

Records donated to Harvard University by the estate of Dr. Clemens E. Benda, Medical Director at Fernald during the time period, allowed the positive identification of the 57 subjects in the Calcium studies. The subjects' names were all recorded by number, and there were specific research notes within the primary researcher's progress reports. Records within the doctoral dissertation archives at MIT allowed the positive identification of the 17 subjects in the Iron study. Again, the primary researcher's notes gave us the subjects' names along with exact experimentation data.

However, in the case of the Thyroid studies the Task Force did not find this comparable level of original research records. The Task Force was forced to base its preliminary analysis, as presented in this report, on the limited information found in the published journal articles. For the radioiodine studies at Wrentham, the Task Force has found only 23 sets of initials and birth dates out of a total of between 104-167 subjects (depending on whether or not the Task Force can determine what, if any, of the subject data were used in both studies). By comparing all identified records of all the residents from that time period whose birth year fell within those approximate age ranges, and by matching that group's names with the identified initials of subjects in published articles, the Task Force has, to date, positively identified only 12 potential subjects.

In a like fashion, the Thyroid study at Fernald has required an identical search of all residents within that time frame against a listing of ages and initials. The search for the positive identification of subjects is still ongoing.

Why was the Task Force able to secure such detailed information on the Calcium and Iron studies and not on the Thyroid studies? The Calcium and Iron studies were nutritional studies that were done by the primary researchers as doctoral dissertations, and the records were kept for sentimental and academic reasons. The Thyroid studies were just one of many research studies done by persons and institutions, and the records were lost or destroyed within this 30- to 40-plus-year time span.

No laws or policies existed at the time that required specific records be kept at the site of the research studies or entered in the subjects' medical records. Researchers had complete discretion in record keeping during and after any study. All of the researchers whom the Task Force was able to identify and contact revealed that they had not maintained records of any studies they had conducted or participated in from that time period.

The following subcommittees were formed to work on specific areas of consideration:

■ **Information Request Subcommittee (David White-Lief, Chair)**

Archival records revealed that close proximity to researchers, universities, and hospitals, as well as the supervised living conditions at an institutionalized setting, were among the primary reasons Fernald had been attractive as a place to conduct studies for the Boston research community. Also, two archival records addressed the unique opportunities for research that institutionalized settings offered and called for specific research on the causes and treatment of medical conditions found in such settings. The archival records indicated medical research of a varying nature was an ongoing component of daily life at Fernald and other institutionalized settings. This subcommittee was formed to request an archival search, with a follow-up report to the Task Force on any studies identified in that search, by all major universities and hospitals in Massachusetts to assure that unpublished research was not missed in the Task Force's review.

Follow-up letters were sent to those institutions failing to submit a report on the date requested. As of the writing of this report, of the thirty institutions contacted, all but four have responded (see Appendix C for a copy of the letter sent and a listing of the institutions contacted; a notation is made next to the nonrespondents).

Requests for any federal agencies' records or reviews were coordinated through Senator Kennedy's and Congressman Markey's offices on behalf of the Task Force. The Department of Energy assigned Dr. George Gebus to serve as a direct liaison for the Task Force.

■ **Narratives Subcommittee (Dr. Gunnar Dybwad, Chair)**

The Task Force decided this report must include a section in which the two former residents and two of the family members who served on the Task Force offer their personal insights and experiences at the time of these studies. These personal statements can be found in the "How Could It Have Happened?" section.

■ **Methodology Subcommittee (Richard Krant, Chair)**

The Task Force required assurance that all other facilities operated by the Department of Mental Retardation were conducting identical searches in a systematic manner. This subcommittee was formed to contact each facility and report to the Task Force as a whole on this effort. See Appendix D for its report.

A review of a random sample of all the archival records was considered for inclusion in this report. The Task Force decided against doing this type of review for the following reasons:

- A representative sample would be difficult to obtain and the results would likely be inconclusive because specific references in residents' records to the subject testing were sparse at best;
- Formal record-keeping policies did not exist in the 1940s through early 1960s;
- Any meaningful review of the archival records must consist of a page-by-page search to assure that any notations within the staff notes are found. The Task Force estimates that 8,000-10,000 individuals have been residents at the Fernald facility alone, with each person's permanent record ranging in size from the oldest (and smallest) filling a single file folder to the more recent records (which have specific, mandated record-keeping guidelines) filling an average of four file folders. However, an example of the extreme was found with a current resident's record filling one entire filing cabinet drawer; and
- When the Task Force reviewed the records of those persons who were positively identified as having been a research subject, no standardized or obvious notation concerning the study was found.

To determine whether or not professionals in the statistical field would agree with the Task Force's belief that these variables would negate the advisability of a random sample it was decided to consult outside experts.

The Task Force sought the opinion of two statisticians: Dr. Monroe G. Sirken, from the Centers for Disease Control and Prevention, and Dr. Nancy Veeder, from the Boston College Graduate School of Social Work. Given the scope and time limitations facing the Task Force, they concurred that a page-by-page review for a random sample would be impractical and of little utility at this time. Instead, a "nonprobability purposive sample" was suggested. However, the Task Force voted to maintain the right to recommend an inclusive, individual record review in the future should it be deemed appropriate.

■ Contact with Subjects Subcommittee (Dr. Anne Howard, Chair)

Discussion within the Task Force indicated that there were serious ethical, psychosocial, and medical issues that needed to be considered before it could be decided when and how to relate the Task Force findings to the identified subjects. The specific areas for consideration and this subcommittee's preliminary recommendations can be found in Appendix E. However, a few key areas of investigation and discussion are highlighted below.

The Task Force was confronted with the question of when and how to respond to inquiries, as well as how to contact those who could be positively identified as a subject in a research study. The issue was whether to inform them immediately or wait until final data and opinions by the radiation and epidemiology experts provided specific information that could be shared with the subjects and their primary physicians at the same time they received notification of their involvement. Our decision was influenced by the two Task Force members who had been members of the Science Club at Fernald. They offered an impassioned plea to wait until specific information was available to share, recounting the terrible effect of uncertainty on their lives. The Task Force decided that the same anxiety must not be inflicted on others. This could be avoided by waiting until complete information regarding the research study details and the potential long-term effects could be communicated.

Many persons who were residents at Fernald for the societal and cultural reasons outlined in the "Introduction" section spent their subsequent lives concealing their pasts as residents from their family, friends, and coworkers. This arose out of the very real concern that upon learning that they had been residents at this facility, people would assume they were mentally retarded. This would cause that person to have to live with the severe stigma that is attached to that label in our culture. In fact, this very scenario has occurred in the lives of the two Task Force members who came forward to offer their insight as former members of the Science Club.

Therefore, the question arose as to whether or not it would be appropriate to initiate contact with all subjects, regardless of their desire to distance themselves from their past as residents of Fernald. What methods must be

used to assure their right to privacy? The Task Force had passed a unanimous motion that the Department of Mental Retardation had a "duty to inform" each research subject identified. Did this "duty to inform" override the subjects' right to privacy and/or their desire not to be associated with Fernald in their present lives? A pivotal question became just how much, if any, medical risk had been incurred as a result of any of the identified studies that used radioisotope tracers.

The Task Force sought the opinion of five outside experts in radiation and epidemiology in an attempt to determine the potential medical risks associated with each of the identified studies and the differing levels of radiation exposure. These opinions can be found in Appendix G. All five experts agreed that there were significantly differing exposure levels for those involved with the nutritional research studies versus those who had been involved in the Thyroid studies.

Reassurance was given to the Task Force on the minimal exposure in the nutritional tracer studies, but serious concern has been raised concerning the Thyroid studies. Furthermore, it was noted by the Task Force that there is a school of thought that there is no such thing as an "acceptable" exposure level. Additional discussions with members of the medical community convinced the Task Force that it was beyond the scope and ability of this group's expertise to handle the depth of discussion associated with the risk that the Thyroid studies deserved within the time frame established for the creation of this report. Therefore, a working group within the Department of Mental Retardation is currently being formed with a mandate to design and coordinate a specific set of tasks: to review and present a policy statement on the issue of medical risk for the Thyroid studies; to create a policy and procedure for contacting and sharing information with persons identified as having been research subjects; and to continue the work of identifying other types of research that had been done in state-operated facilities. This working group is being formed as this report goes to press.

Please Note

When reviewing the records of former residents of the state-operated facilities, the Task Force became concerned with the archaic, degrading, and judgmental language that was the standard medical terminology of the day.

Terms such as "moron," "idiot," "fool," and "imbecile," as well as judgments and descriptions concerning family members, makes these archival records insulting and controversial.

A letter of apology and explanation was drafted to accompany any records requested by former residents and their families. The letter is reproduced on the opposite page.



The Commonwealth of Massachusetts
 Executive Office of Health & Human Services
 Department of Mental Retardation
 160 North Washington Street
 Boston, MA 02114

Philip Campbell
 Commissioner

Area Code (617)
 727-5608
 TDD Line
 727-9866

Dear , :

Enclosed you will find the complete set of records we have in our file for [NAME] including a xerox of a photograph that was taken of them as a resident; any immunization, medical, and dental records; and, any birth, confirmation or baptismal records we could locate.

Before you read the records, I wanted to personally apologize for the archaic, and frankly, insulting language of that era that you may find in this old records. The use of the terms such as "moron", "imbecile" or "idiot" were actually the standard medical terminology of the day. However, the use of such terms is appalling to those of us who serve citizens who are retarded today.

Also, it is important to note that not all residents of Fernald were admitted due to mental retardation. Society allowed many persons to be admitted to Fernald School for a multitude of reasons aside from mental retardation and no one should assume that they are mentally retarded just by virtue of their having been a student here.

There is also a possibility you will see similarly disparaging language or reporting on the parents of our former residents/students. Please understand that it was the type of judgement and categorization allowed at that time. However, it can be very upsetting to read today by our former residents, their spouses, children, or significant others.

Again, please accept my sincere apologies for any disturbing language you find and know that we are working diligently today to assure the dignity of all of our citizens, residents and consumers served by the Department of Mental Retardation do not face such derogatory language or treatment again.

Very truly yours,

Philip Campbell
 Commissioner

WHAT HAPPENED?

Of significant note is that no research was identified by the Task Force that involved testing the effect of radiation on human beings by introducing radioactive materials purposefully into their bodies to measure or monitor such effects. The nutritional research studies used small amounts of radioactive material as tracer elements to understand how the body functioned or obtained elements from the diet; the Thyroid studies used small to large amounts of tracer materials, also to learn about body functions; and, the so-called Cold War study at Wrentham differed in that the tracer materials were used to find the point at which administration of iodine blocked the uptake of radioactive materials that would be found in nuclear fallout.

Nutritional Research Studies

- 1946 Iron Study
17 subjects: all identified
- 1950-53 Calcium Studies
17 separate experiments done over three years
57 subjects total: all identified
- 1955 Radioactive Calcium Study
Proposed but no confirming records found
33 potential subjects: all identified

Thyroid Studies

- 1952 Thyroid Function in Myotonia Dystrophica
6 subjects: identities still undetermined
- 1957 Thyroid Function in Down Syndrome: Fernald
28 subjects: identities still undetermined
- 1961 Nuclear Fallout Study: Wrentham
70 subjects: identifies still undetermined
- 1961 Thyroid Function in Down Syndrome: Wrentham
104-167 subjects: 12 identified to date

Therapeutic/Diagnostic Use of Radioactive Isotopes

- 1962-73 Five archival records were found documenting
tracer studies or the therapeutic use of
radioactive materials involving residents with
specific metabolic disorders
-

To address the issue of the potential risk incurred by these dosage levels, five opinions by experts within the fields of radiation and epidemiology have been included to outline an assessment of that risk factor. The full text of these opinions can be found in Appendix G. Also, a brief summary of the nature of ionizing radiation and what is meant by the effective whole body dose equivalents is included in Appendix F.

■ Research Studies Identified by the Task Force

This section contains all of the facts that the Task Force has been able to identify, as of this time, concerning the research studies that involved residents at two Massachusetts state schools: Fernald and Wrentham. Many of the findings and discussions in other sections of the report are based on the material presented in this and the next section, "Archival Record Chronology." The information is presented objectively, including only those notes necessary to assist the reader by clarifying or expanding the information being presented. The chart on the previous page summarizes all of the studies found. A study-by-study outline follows.

The research studies are grouped into the following three categories:

■ Nutritional Research Studies

Two nutritional research studies were done that used radioactive iron (1946) and radioactive calcium (1950-53) as metabolic tracers. Both research studies were carried out using Fernald residents as subjects. These are the two studies that archival records have allowed this report to present in great detail. The Task Force can positively identify all of the subjects from these studies and have found the six journal articles that arose from them.

■ Thyroid Studies

Throughout the 1950s and 1960s there were three identified research studies in which radioactive iodine was used as a tracer to understand the function of the thyroid gland. These appear to have involved residents of Fernald, family members of Fernald residents, and residents of Wrentham. However, the amount and type of tracer materials used went beyond the minimal tracer levels of the nutritional research studies and into levels that create concern for the need of follow-up medical and epidemiological study. The Task Force will allow the follow-up working group to conduct that next level of research and analysis for reporting at a later date and so will not focus on these studies in this report.

One Thyroid study in 1961 stood out from the others. This was a study, using children who were residents of Wrentham, to determine how much normal iodine was needed to be added to the diet of children to block the uptake of radioactive iodine from fallout following a nuclear attack or accident. This study can be called a Cold War experiment and stands alone in fitting that categorization. The Task Force learned that the results of this study were actually referenced at a 1989 European conference after the nuclear accident at Chernobyl.

■ Therapeutic/Diagnostic Use of Radioactive Isotopes

Archival records were found that dealt with the use of radioactive isotopes for therapeutic or diagnostic testing on a select number of residents who had specific medical conditions.

■ Nutritional Research Studies

During the time period leading up to and surrounding these studies, the focus of experimentation nationally had shifted in part to nutritional and digestive issues relating to malnutrition and feeding of large populations: "The study of human digestion was a major focus of American medical research [and] metabolic studies of both normal and sick children were also reported...As early as the 1870s, physicians used dyes and other chemicals for gastrointestinal studies in adults. Beginning about 1909 pediatricians conducted similar studies in infants and children."¹

The purpose of the research involving the residents at Fernald was to understand how the body obtained the minerals iron and calcium from dietary sources and to find out whether compounds in cereals affected their absorption. It had been known from nutritional studies of bread in the late 1930s that a class of chemical compounds, inositol hexaphosphates (commonly called phytates), could form insoluble compounds with iron to prevent its absorption from food. Phytates are commonly located in the outer covering (integument) of grain and were present in poorly milled white flour. Some cereals (e.g., rolled oats) contained phytates; others (e.g., farina, commonly known as Cream of Wheat) did not. The immediate goal of the research was to understand if either of these cereals was preferable from a nutritional point of view.

□ **Iron Study: 1946**

This study involved 17 subjects who received seven breakfasts, each with a minute amount of radioactive iron as a tracer mixed into the milk that was served over the cereal. The subjects received the first five breakfasts over a period of about 12 weeks. After a wait of 25 weeks, they received two more breakfasts: the sixth at week number 37 and the seventh at week number 40.

Calculating the dose was complicated, because different amounts of iron were absorbed from each breakfast, and two different kinds of radioactive iron were used (⁵⁵Fe and ⁵⁹Fe). However, there was sufficient information available in the single published article² as well as in the doctoral thesis of Dr. Leonard M. Sharpe, submitted to the Task Force by the Massachusetts Institute of Technology (MIT), to permit this calculation.

The chart (see Figure 1) shows the amount of radiation each subject received from participation in the Iron study, along with the 300 millirem annual effective whole body dose equivalent of radiation from natural background sources in the Boston area. For comparison, the higher 400 millirem natural background dose received by a resident of Denver is also shown.

The researchers were from MIT and Fernald. The research was supported by the Quaker Oats Company.

□ **Calcium Studies: 1950-53**

The same motivation for understanding the role and impact of phytates was the foundation for this study, but the researchers now used a minute amount of radioactive calcium tracer. This study involved 15 subexperiments conducted over a three-year time frame and served as the basis for five published articles.

The best knowledge of this research comes from Dr. Felix Bronner's doctoral thesis. A series of progress notes that had been sent to Dr. Clemens E. Benda, Medical Director at Fernald at that time, were secured from the

¹M.A. Grodin and L.E. Glantz, *Children as Research Subjects: Science, Ethics & Law* (New York City: Oxford University Press), 1993, p.9.

²L.M. Sharpe, W.C. Peacock, R.Cooke, and R.S. Harris, "The Effect of Phytate and Other Food Factors on Iron Absorption," *J.Nutrition* 41, 433-446 (1950).

papers donated by his estate to Harvard University. Three of the published articles^{3 4 5} also contained substantial information that allowed these calculations.

In the main set of experiments, there was a total of 54 subjects, who were listed only by weight and age in the appendix of Bronner's thesis. There were 8 subjects who were not mentioned in the published articles but were noted in the progress report as having served as controls. The next 36 subjects received two breakfasts with 0.85 microcuries of ⁴⁵CA in each. Another 9 subjects each received a single injection of 0.75 microcuries of ⁴⁵CA, as well as a single breakfast containing an additional 0.85 microcuries of ⁴⁵CA. These subjects each weighed between 63 and 92 pounds and received 1.0 microcuries of ⁴⁵CA orally. The effective whole body dose equivalents they received ranged from 6.4 to 4.4 millirems. There was 1 unidentified adult who also received an injection containing 2.02 microcuries of ⁴⁵CA. The final 3 subjects (for the final total of 57 subjects overall) were not involved in the main set of experiments but received a single injection each for a "long-term follow-up study."

The largest effective whole body dose equivalent received by any of the subjects was 15 millirems, and the smallest was 4 millirems. Figure 1 illustrates the amount of radiation each subject received from participation in the Calcium studies, along with the dose equivalent of radiation from natural background sources in the Boston and Denver areas as previously discussed. For comparison, the doses persons receive today in common medical diagnostic procedures, ranging from a chest X-ray to a brain scan, are also given in a third chart.

One of the subexperiments within the calcium metabolism study involved a 10-year-old patient who was terminally ill with Hurler-Hunter syndrome (which in that time period was also referred to by the archaic and unacceptable term "gargoylism"), a degenerative disease of the nervous system associated with defective mucopolysaccharide metabolism. The patient was given 80 microcuries of ⁴⁵CA and was found to have abnormal calcium metabolism, but he died before the study could be completed.

The researchers were from MIT, the Harvard Medical School, and Fernald. The research was supported by the Quaker Oats Company and the Atomic Energy Commission.

The risk assessment done by Dr. Joseph L. Lyon, an outside epidemiologist with a specialty in radiation medicine (see full text in Appendix G), was very reassuring to the Task Force on these nutritional research studies. Dr. Lyon not only concurred with the dosimetry done by Dr. Litster (also in Appendix G), and supported the findings of the other three expert opinions received, but he was also able, as an epidemiologist, to state that "children exposed to ionizing radiation generally manifest the excess risk of leukemia in the first 15 years after the exposure." Between 40 to 50 years have now passed since these research studies were done, allowing Dr. Lyon to speculate that if the subjects did not exhibit a leukemia between 1961-1970, then it is unlikely that they would suffer this most severe of potential medical risks from either the Calcium or Iron tracer studies.

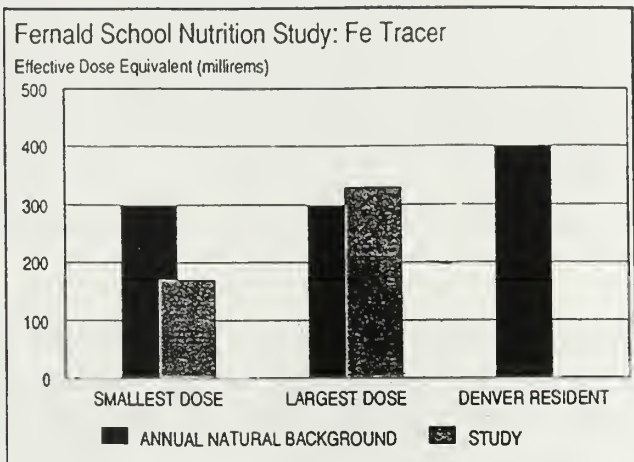
³F. Bronner, R.S. Harris, C.J. Maletskos, and C.E. Benda, "Studies in Calcium Metabolism. Effect of Food Phytates on CA⁴⁵ Uptake in Children on Low-Calcium Breakfasts," *J.Nutrition* 54, 523-542 (1954) .

⁴F. Bronner, R.S. Harris, C.J. Maletskos, and C.E. Benda, "Studies in Calcium Metabolism. Effect of Food Phytates on ⁴⁵CA Uptake in Boys on a Moderate Calcium Breakfast," *J.Nutrition* 59, 393-406 (1956) .

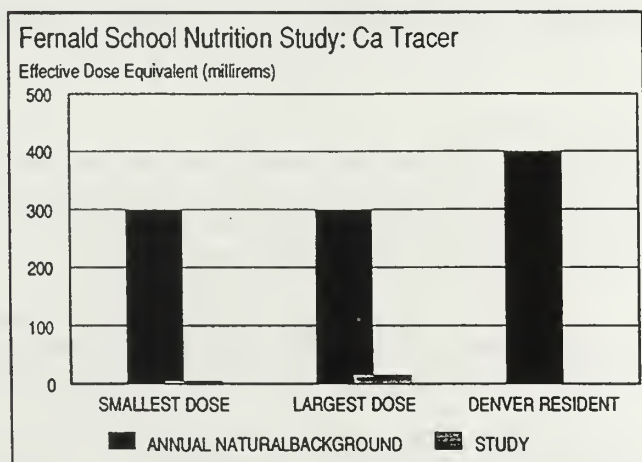
⁵F. Bronner, R.S. Harris, C.J. Maletskos, and C.E. Benda, "Studies in Calcium Metabolism. The Fate of Intravenously Injected Radiocalcium in Human Beings," *J.Clin.Invest.* 35, 78-88 (1956) .

Figure 1: Calcium & Iron Studies Compared with Annual Background Exposure to Radiation in Boston, in Denver, and in Common Medical Procedures

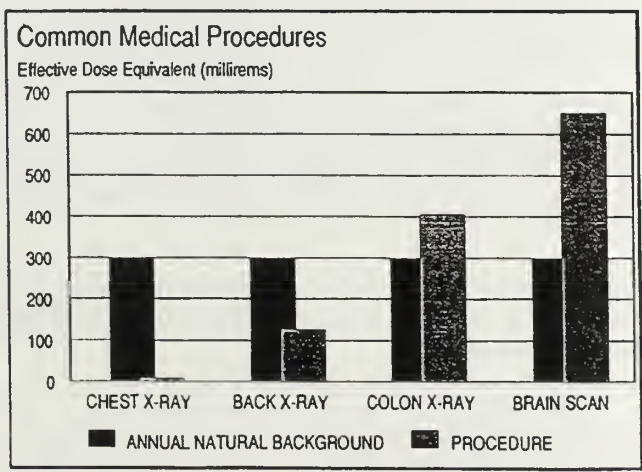
1946
IRON STUDY



1950-53
CALCIUM
STUDY



COMMON
MEDICAL
PROCEDURES



SPECIAL NOTE: During the archival review, the Task Force compiled a comprehensive set of records that address key areas of concern. These include an outline of the understanding of tracer studies in the 1940s; the rationale for the nutritional research studies; reasons the studies were done at Fernald; the existing policies and guidelines for conducting research on human subjects in that era, including steps taken by the researchers to gain permission from the state and federal authorities to conduct the research; and the methods used to obtain consent from parents/guardians. Permission for wards of the state to participate was given by the superintendent of the institution. An outline of the contents of these records is in the following section, "Archival Record Chronology," and copies of the original archival records can be found in Appendix B.

■ Thyroid Studies

Unlike the nutritional research studies, this report will not contain dose interpretation or risk assessment for the Thyroid studies. This will be conducted by the follow-up working group.

☐ **Nuclear Fallout Study: Wrentham**

This study was singled out for special and immediate treatment due to the nature of the study. A press release was issued by the Task Force on February 8, 1994, alerting the public to its discovery. Studies of this nature fall under what society has come to call "Cold War experiments," focusing on the medical effects a civilian population will suffer from fallout following a nuclear attack or accident.

The body requires iodine as a nutrient, and uptake of the small amounts normally present in the diet is high. The purpose of this study was to determine how much normal iodine was needed to be added to the diet of children to block the uptake of radioactive iodine they might be exposed to from nuclear fallout.

The study⁶ involved 70 subjects, who ranging in age from 1 to 11 who were residents of the Wrentham School. The 63 primary subjects were given daily dietary supplements of stable (nonradioactive) sodium iodide, ranging from 100 micrograms to 1,000 micrograms, for a period of 12 weeks. An additional 7 subjects were given a single dose of 1,500 micrograms per square meter of body surface of stable iodide.

Radioactive iodine, ¹³¹I, was given as a tracer to measure the rate of uptake of stable dietary iodine. One of the researchers has since died and the other two were unable to provide any significant additional details, but it appears from Figure 1 of the article⁷ that 1 microcurie of ¹³¹I was given to 5 2-year-old subjects every 2 weeks for 14 weeks. Thus, each subject received a total of 8 microcuries of ¹³¹I. Similar doses were probably given to the other subjects in the study.

The researchers were from the Harvard Medical School, Massachusetts General Hospital, and the Boston University School of Medicine. The research was supported by the Division of Radiological Health, Research Branch, of the U.S. Public Health Service.

⁶K.M. Saxena, E.M. Chapman, and C.V. Pyles, "Minimal Dosage of Iodide Required to Suppress Uptake of Iodine-131 by Normal Thyroid," *Science* **138**, 430-31 (1962).

⁷ Ibid.

The Task Force has been informed by the outside experts that the stable iodine should have posed no risk in and of itself as it is a normal dietary requirement. Literature cited in the journal article arising from this study stated that even unusually high levels of ordinary iodine would only pose problems if administered for several years. With enriched flour and other foods, the modern diet can easily include about 1,000 micrograms per day of iodide.

Of concern, however, is the dose of the radioactive iodine to the thyroid gland and the potential for the subjects to have developed thyroid nodules and cancers. Previous studies, completely unrelated to residents of these state-operated facilities, had shown that some children treated with large doses of X-rays to the head and neck developed both. Yet, in other nationally published studies, injection of ^{131}I has appeared to be about three times less likely than an equivalent external dose of X-rays to produce disease, probably because the dose is spread out in time and is less uniformly distributed in the thyroid.

Further investigation revealed a large epidemiological study of 35,074 patients in Sweden⁸ who were given ^{131}I for diagnostic purposes. The patients did not show an increase from the normal risk of cancer found nationally after periods of 10 to 20 years. The average dose to the thyroid gland in the Swedish studies was 50 rads, about the same as the maximum dose to any subject in the Wrentham study. Yet, again, opposing statistics were found in a second large epidemiological study⁹ of persons living in the United States who were followed for evidence of thyroid disease as a result of exposure to radioactive fallout from weapons testing. These subjects did show an increase in the percentage of thyroid disease above the expected range.

Clearly, there is no definitive theory as to the absolute long-term risk in the area of ^{131}I exposure. Wanting to err on the side of not ignoring any potential for risk, one of the authors of this latter study, Dr. Lyon, was one of the experts called upon for an opinion of risk assessment on the nutritional research studies for this report.

☐ **Thyroid Function in Down Syndrome: Wrentham**

There was a second study published in 1965¹⁰ by two of the three authors of the Wrentham nuclear fallout study noted above. From conversations the Project Coordinator had with Dr. Saxena, this second study was created with some degree of overlap in subject data. The purpose was to test the thyroid function in children with Down syndrome and to compare it with children whose thyroid function was normal.

The study involved 53 children with Down syndrome, along with 51 other children with mental retardation of other etiology from Wrentham: ages ranged from 1 through 15. The published article does not give information on the dose of radioisotopes the subjects may have received. Neither Dr. Saxena nor Dr. Pryles have any records from that study still in their possession.

The conclusion from the research was that iodine uptake and plasma levels of thyroid hormones were within the normal range for these subjects. The researchers also concluded that red blood cell uptake of the thyroid hormone triiodothyronine labeled with ^{131}I could be used as a test of thyroid function. This was an in vitro test and did not require giving radioactive iodine to the children.

The researchers were from the Harvard Medical School, Massachusetts General Hospital, and the Boston University School of Medicine. The research was supported by the Division of Radiological Health, Research Branch, of the U.S. Public Health Service.

⁸ L.E. Horn, K.E. Wiklund, G.E. Lundel, N.A. Bergman, G. Bjelkengren, U.C. Ericsson, E.S. Cederquist, M.E. Lidberg, H.V. Wicklund, and J.D. Boice, Jr., "Cancer Risk in Population Examined with Doses of I-131," *J. Nat. Cancer Inst.* 81, 302-306 (1989).

⁹ - "A Cohort Study of Thyroid Disease in Relation to Fallout from Nuclear Weapons Testing," *JAMA* 270, 2076-2082 (1993).

¹⁰ K.M. Saxena and C.V. Pryles, "Thyroid Function in Mongolism," *J. Pediatrics* 67, 363-370 (1965).

☐ **Thyroid Function in Myotonia Dystrophica**

This research involved a study at Beth Israel Hospital of thyroid function in 6 patients with myotonia dystrophica,¹¹ a severe chronic neurological disorder. Thyroid pathology had been observed to accompany this disease, but the relation between myotonia dystrophica and thyroid problems was unknown. The goal of this study was to clarify the situation.

The 6 patients were all male and are identified by their initials in the published article but their ages are not given. The only indication they might be connected with Fernald is that Dr. Benda, the Medical Director for Fernald at that time, was the first author of the published article. Just as this report was going to press, the Task Force had received additional papers directly from the Benda estate, and there appears to be more definitive and identifying information available to the follow-up working group.

The conclusion was that thyroid function in these subjects, as measured by uptake of the radioactive tracer, was within the normal range. As pathology reports indicated that the thyroid gland was found to be larger than normal in most patients with myotonia dystrophica, the authors concluded that in patients with this disease the thyroid gland operates at a lower than normal capacity, but the capacity is sufficient to maintain an output that is clinically, biophysically, and biochemically within normal range.

The researchers were from MIT, the Harvard Medical School, and Fernald. The research was supported by the Atomic Energy Commission and other unidentified sponsors.

☐ **Thyroid Function in Down Syndrome: Fernald**

At the time of this study, the origin of Down syndrome (mongolism was the archaic and unacceptable term used for this syndrome at that time) was unknown, but children with this condition were reported to have abnormal thyroid glands, as were their mothers. The purpose of this research¹² was to examine thyroid function in 21 residents at Fernald as well as in 7 parents. The parents who were used as subjects in this study did not necessarily their own children participating in this study but had been recruited by Dr. Benda who knew them as parents from Fernald.

The level of radioactive iodine tracer ¹³¹I used in the study, again, caused the Task Force serious concern and will be a key study in the follow-up analysis being done by the working group.

The conclusion was that thyroid function in both the subjects with Down syndrome and the parents was normal. Those with Down syndrome demonstrated higher turnover rates of iodine, which suggested that a smaller effective portion of the thyroid gland was working at an intense rate in order to maintain normal levels of thyroid hormones.

The researchers were from Harvard Medical School and the Beth Israel Hospital. The research was supported by the National Institute of Arthritis and Metabolic Diseases and the Atomic Energy Commission.

¹¹C.E. Benda, C.J. Maletskos, J.C. Hutchinson, and E.B. Thomas, "Studies of Thyroid Function in Myotonia Dystrophica," *Am.J. of Medical Sciences* 228, 668-672 (1954).

¹²G.S. Kurland, J.Fishman, M.W. Hamolsky, and A.S. Freedberg, "Radioisotope Study of Thyroid Function in 21 Mongoloid Subjects, including Observations in 7 Parents," *J.Clin. Endoc. and Metab.* 17, 552-560 (1957).

Archival Record Chronology

This section presents a chronology of events and facts leading up to and encompassing the Iron and Calcium studies that were done using Fernald School residents as subjects. They are reproduced here in their entirety to allow full disclosure of all the facts found. Copies of the actual archival letters and reports referred to in this chronology may be found in Appendix B.

LEGEND OF MAJOR NAMES FOUND IN THIS CHRONOLOGY

AEC	Atomic Energy Commission
DMH	Department of Mental Health
F	Fernald School
MIT	Massachusetts Institute of Technology
NBL	Nutritional Biochemistry Laboratories, MIT
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Abersold	Dr. Paul C. Abersold, Isotopes Branch, AEC
Benda	Dr. Clemens E. Benda, Medical Director, Fernald
Bronner	Dr. Felix Bronner, Primary Researcher in the Calcium studies for his doctoral thesis, MIT
Evans	Dr. Robley D. Evans, Professor of Physics, MIT
Farrell	Dr. Malcolm J. Farrell, Superintendent, Fernald
Harris	Dr. Robert S. Harris, Director, NBL, MIT
Lough	S. Allan Lough, Chief, Radioisotopes Branch, AEC
Perkins	Dr. Clifton T. Perkins, Commissioner, DMH
Sharpe	Dr. Leon M. Sharpe, Primary Researcher in the Iron studies for his doctoral thesis, MIT
Tadgell	Dr. Henry Tadgell, Superintendent, Belchertown, and Secretary to the DMH Advisory Committee on Psychiatric Education and Research
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The use of this symbol shows an archival record the Task Force felt to be of special significance.

1945

July 1, 1944-June 30, 1945 (Appendix B-1)

Report of Progress in Research/MIT: NBL annual report announcing their intended study of "Effect of Phytates upon the Absorption and Excretion of Calcium, Phosphorus and Iron," on page 15 of the report.

December 19, 1945 (Appendix B-2)

✉ Correspondence from Harris (MIT) to Farrell (F) identifying the general reasons for the studies contemplated and why Fernald was selected as the site. Most illuminating are references to the advantages of conducting such experiments with institutionalized populations.

Nutritional scientists had been alerted by animal research which suggested that phytates in cereal products block absorption of calcium and iron. It is stated in this letter that initially animal studies would be carried out to work on experimental techniques and to establish procedures. However, to examine the role of phytates in the human diet, it was desirable to study children who ingested standardized diets in a controlled setting; hence, the decision to use residents of Fernald. Fernald's proximity to universities is also mentioned as a reason for its selection.

Harris notes that radioactive iron tracers would be used and explains that radioactive minerals are metabolized in the same manner as nonradioactive forms and thereby could be used to trace the metabolic process in the human body. In other words, a small "tracer" dose of radioactive iron would be added to ordinary nonradioactive iron in phytate-containing cereal that would be served to the subjects as part of their breakfast meals.

The dosage of radiation intended to be received by the subjects would "emit less energy than from the cosmic rays continually bombarding people living at the altitude of Denver, Colorado." A two-year follow-up study of medical students who had received three to five times the dosage of radioactive substances revealed that "there is absolutely no ground for caution regarding the quantities of radioactive substances which we would use in our experiments."

✉ (Note: A draft of a letter from Evans [MIT] to Abersold [AEC] is included in B-2/A because it gives a good summary of the current thought on the risks associated with the use of radioactivity in the 1940s.)

For one month prior to the beginning of the study, vitamins would be administered to the subjects to ensure that vitamin deficiencies would not influence the studies. Harris also offered "if there is any way in which we can reward our subjects, we would be glad to do so." The letter ends by noting that "the results of this investigation will be of great importance and will influence our thinking in terms of the nutrition of mankind."

(Note: Interestingly, during the review process a letter was found concerning the recruitment of subjects noting that the researchers preferred male subjects to female subjects due to the "issues of collecting urine and stool specimens." However, it was stated that if enough males had not been identified, they would have used females. This was not the case and no female subjects were used in this study.)

December 27, 1945 (Appendix B-3)

✉ Correspondence from Perkins (DMH) to Farrell (F) appears to show that the proposed iron tracer study was actually the first research done at Fernald with outside collaborators, for Perkins writes: "Perhaps you have not yet become familiar with our procedures in research activities. These proposed activities go through the Advisory Council on Research and Teaching."

This is also the first evidence the Task Force found that some method had been established for review and approval of proposed research studies involving the residents of Fernald. Farrell is advised to contact the council. It appears that there is little likelihood the project would be rejected, however, for Perkins advises Farrell to go ahead and select the "fifteen or so patients" and to get the "necessary family approvals." Farrell is given permission to start administering the prestudy vitamins for the next month.


December 29, 1945 (Appendix B-4)

Correspondence from Tadgell (DMH) to Farrell (F) informing him that the proposed research study will be

brought before the committee and inviting him to attend the meeting.

1946

March 29, 1946 (*Appendix B-5*)

 Correspondence from Perkins (DMH) to Farrell (F) noting that the Advisory Committee unanimously approved the proposed iron tracer research, that the Department of Mental Health concurred, and that he was free to proceed "in the research at the full and proper level."

July 1, 1945-June 30, 1946 (*Appendix B-6*)

Report of Progress in Research/MIT: NBL annual report confirming that the iron and calcium components of the research proposal have now been divided into two separate studies and that the Iron study has been chosen to be done first.

1948

July 1, 1946-June 30, 1948 (*Appendix B-7*)

Report of Progress in Research/MIT: NBL annual report showing the findings of the Iron study and announcing that the Calcium study (to be called "Effect of Phytates upon the Absorption of Radioactive Calcium") is now in the planning stage. It is noted that animal studies will be done first to prove that radioactive calcium is not toxic for human beings.

1949

March 23, 1949 (*Appendix B-8*)

Correspondence from Harris (MIT) to Benda (F) enclosing an outline of the research experiment using radioactive calcium that had been discussed with him at a luncheon the week before. Another luncheon for further discussion with Evans (MIT) is offered. A copy of this original outline was not found.

April 13, 1949 (*Appendix B-9*)

Correspondence from Harris (MIT) to Benda (F) concerning the revised outline and setting a time and date for the luncheon discussed in the previous letter. A copy of the revised outline is included in B-9/A.

April 20, 1949 (*Appendix B-10*)

Correspondence from Benda (F) to Tadgell (DMH) requesting the DMH Advisory Committee (whose function was to review any research proposals) consider the Calcium study proposal. Benda states that "the study does not include any danger to the life or health of the patient" and that it "appears desirable" to get the committee's approval. He also notes the previous approval of a similar study, presumably the one using radioactive iron.

April 26, 1949 (*Appendix B-11*)

Correspondence from Joel B. Bulkley (MIT) to Benda (F) sending him copies of AEC Form 313 prepared for his signature, a copy of a letter from Evans (MIT) to attach to the final set of forms, and a reminder set of instructions on what he must do to complete the AEC application process. This is presumably a request for the radioactive calcium isotope. (Note: The isotopes used in the earlier Iron study were made in the MIT Cyclotron.)

May 7, 1949 (*Appendix B-12*)


Correspondence from Tadgell (DMH) to Farrell (F) notifying him that the protocol for the proposed Calcium study had been presented to the DMH Advisory Committee and after "a goodly amount of discussion" it was voted to defer approval until it was further discussed at the next meeting. Benda (F) was invited to attend to discuss "any questions that may arise." (Note: The Task Force searched for, but did not find, any minutes or correspondence to clarify the discussion held at the Advisory Committee meeting.)

May 18, 1949 (*Appendix B-13*)

Correspondence from Farrell (F) to Abersold (AEC) confirming the formation of an Isotopes Committee and, as its chairman, giving his approval of the proposed calcium research. This is part of the process requested by the AEC as referred to in Bulkley's (MIT) earlier correspondence (April 26, 1949).

On the next page (B-13/A) Benda (F) has sent to Abersold a list of the names of this new committee to comply with the AEC requirements. The membership included Farrell, Benda, Dr. Maximilian Weinberger (an assistant physician), and Dr. Elizabeth Belmont (a physician), all from Fernald, and Dr. Earle Chapman from Harvard Medical School. The committee's responsibility was to "supervise the proposed research."

June 8, 1949 (Appendix B-14)

 Correspondence from Tadgell (DMH) to Farrell (F) announcing that the DMH Advisory Committee gave unanimous approval to the Calcium study's protocol and thanking Benda (F) for attending and answering questions.

September 28, 1949 (Appendix B-15)


Correspondence from Lough (AEC) to Benda (F) providing the authorization number (#3435) for the "procurement of up to three millicuries of ^{45}Ca of high specific activity from the Massachusetts Institute of Technology."


Enclosures noted as attached (included in Appendix B-15/A-C) are:


1. Copy of a letter from Lough (AEC) to Evans (MIT)
2. Form No. 374
3. Form No. 313
4. Certificate No. 3435 (Note: This is the only attachment that was not found.)


(Note: An AEC Order Blank and a listing of AEC documents (B-15/D-E) that were available for purchase through the Technical Information Branch are included because they illustrate the type of studies being conducted nationally at that time which utilized radioactive materials.)


September 28, 1949 (Appendix B-16, 17, & 18)

 Correspondence from Lough (AEC) to Evans (MIT) explaining that the "one irradiated unit of Ca 45" that was applied for (listed as CaCO_3 , item #13A) contains "about three millicuries." (Note: That would be enough for 3,000 doses of one microcurie each.) Evans is advised that he can order smaller, specific amounts that would be adequate for their needs.

 In the third paragraph, Lough refers to the letter sent to Benda (F) mentioned above and notes that the AEC Subcommittee on Human Applications had stipulated that "only one dose of Ca 45 is to be administered to each normal child used in the study." This appears to bear witness that the federal-level Research Advisory Board of the AEC, which reviewed research applications for studies involving human subjects, had also given approval to this study's protocol.

 Appendix B-17, October 27, 1949: Correspondence from Benda (F) to Lough (AEC) stating that although he has apparently consulted with a physicist, he still has a question whether or not the "one dose" the AEC said could be given to a child subject consists of the entire three millicuries. (Note: This would actually be the maximum total amount of material the researchers were authorized to obtain for the whole study.) Benda asks for clarification of the size of the allowed dose.

 Appendix B-18, November 3, 1949: Correspondence from Lough (AEC) --signed by James R. Mason-- to Benda (F) answering his question about dosage. Lough quotes from the original application to the AEC for permission to have the isotopes and reminds Benda that the application stated that no subject would receive more than one microcurie.

 The AEC application also stated the researchers were interested in using subjects in more than one test. The AEC clearly preferred that the subjects receive only one dose of radioactive calcium (not to exceed one microcurie). Recognizing that the researchers wanted to have some of the subjects participate in more than one

study, Lough agrees to allow this for "mentally deficient" subjects provided they did not receive more than the stipulated maximum of one microcurie. He added that the AEC Subcommittee on Human Applications recommended that "normal" control subjects only be allowed to participate in one study with an identical maximum dose of one microcurie.

☞ The letter appears to be evidence that the AEC made a distinction between "normal" and "mentally deficient" subjects in terms of their use in multiple experiments, even though the maximum allowable dose was held the same. No explanation was offered in any of the documents for this distinction.

☞ (Note: The Task Force review did note that most of the subjects received 1.7 microcuries, instead of the 1.0 microcuries permitted by the AEC at that time.)

November 2, 1949 (*Appendix B-19*)

☞ Correspondence from Farrell (F) to the parents/guardians of the proposed subjects requesting permission for their children to participate in the study. Farrell does not include information that there are radioactive tracers involved but highlights the fact that the subjects will have a "special diet" rich in iron and vitamins and implies that there will be "gains in weight and other improvements."

Farrell notes that there will be multiple blood tests, and assures that the tests are the same type the residents had experienced previously and that they would cause "no discomfort." Once again Farrell states there may be possible improvement from participation. He goes on to say that MIT "plans to reward patients taking part." He ends by personally assuring the parents that he feels this project "will be of great importance and that much valuable information concerning nutrition can be obtained which eventually will be of considerable benefit to mankind" and again asks for their cooperation.

1950

March 10, 1950 (*Appendix B-20*)

Correspondence from Harris (MIT) to Farrell (F) giving the results of a one-week survey on the food served to the general population at Fernald. The full results are given with the notation that "the food being served at the Fernald School does pretty well in meeting these estimated requirements" established by the Food and Nutrition Board, National Research Council.

1953

May 1, 1953 (*Appendix B-21*)

☞ Correspondence from Harris (MIT) to Benda (F) outlining the next proposed study "of five different calcium sources." It discusses the need to recruit 15 subjects to participate. Harris writes that Bronner (MIT) had "lined up" ten subjects but "three of these subjects objected to be [*sic*] included in the study and this reduced the number to seven." He further notes that five of the boys who had participated in the earlier study were interested in joining this one; however, they had already received one microcurie of ⁴⁵CA so they would not be able to participate in this new study. It was planned that each subject would participate in five separate experiments within the study, receiving one microcurie in each experiment. (Note: The Task Force could not verify if the AEC did or would have approved that, although records show that the allowable maximum dose was requested to be raised to five microcuries.)

Harris notes that they had "neglected the Fernald Science Club angle"; he suggests a baseball game be lined up. He also asks that an assembly be arranged so they could encourage the boys to participate and to "feel satisfied their small pain is really worthwhile."

(Note: The letter shows two aspects of the "recruitment" process. First, the residents were offered incentives that would be hard for an institutionalized individual to resist. Second, the residents were given some opportunity to decide whether or not to participate in the research study. In conversations with the Project Coordinator, both of the primary researchers from the Iron and Calcium studies expressed a level of personal involvement and

friendship that developed with many of the boys.

It is Dr. Bronner's recollection in one of the conversations that funds were not secured for this particular experiment as outlined and it was not conducted at Fernald after all. Bronner also recalled that the studies were continued on animals. The Task Force secured a copy of a MIT press release from 1957 announcing that Harris received funding for calcium nutrition studies from another source and the subjects would be primates. The Task Force did find an abstract in *Federal Proceedings* [15, 575-76 (1956)] reporting a comparison between human and animal calcium metabolism. It includes primates and the human data results appear to be from the nine boys and one adult subjects from the earlier Calcium injection subexperiment done as a part of the Calcium study.¹³)

May 3, 1953 (Appendix B-22)

Handwritten note from Dr. Kelley (a physician on staff at Fernald) to Benda (F) listing seven boys who had "signified their willingness to participate" as well as five boys "who have previously been in the science tests [and] are willing to participate again if accepted."

(Note: Any archival record that reveals a resident's name is reproduced in this report with the name blocked out to respect the individuals right to confidentiality.)

May 28, 1953 (Appendix B-23)

✉ Correspondence from Benda (F) to the parents/guardians of the proposed subjects requesting permission for participation in the study. Again, there is no indication that radioactive tracers are being used in the studies explained in this letter. Benda states only that the meals will have "a certain amount of calcium." The taking of blood is revealed and "privileges" such as "a baseball game, [a trip] to the beach, and to some outside dinners" are given as incentives/rewards.

✉ Significantly, this letter states that "if you have not expressed any objections [by the given date] we will assume that your son may participate." (Note: The lack of information concerning the use of radioactive material again renders it impossible to obtain informed consent. In addition, no affirmative act was required by a parent for consent to have been assumed. In other words, the act of nonresponse was assumed to provide consent.)

June 5, 1953 (Appendix B-24)

✉ A list of "Science Club Boys" from Boys Hall (BH). Two of the boys have a notation after their names that show a parent/guardian had given permission for their participation, and three other boys had notations of their birth year, mental age, IQ, and weight. There is also a list of names (B-24/A) that had an envelope attached which had been stamped "return to sender." It appears to have been kept in the records to verify the effort to contact that parent/guardian. The Task Force also found a copy of a letter that was marked as having been addressed to both parents, living at separate addresses, which appears to again verify the administrators' efforts to reach either or both parents. (Note: This same method of detailed record keeping of the outreach done and consent forms received, listed by name and relationship, was found for all of the nutritional research studies.)

June 29, 1953 (Appendix B-25)

Correspondence from Benda (F) to a parent regarding her plans to take her son on vacation. It notes that the son is cooperating in a Science Club study and requests that she delay the pick-up for two days due to his participation in the study.


(Note: The letter appears to imply that she was not aware of the dates of the study. The Task Force cannot determine if this was due to her having not been contacted, having been one of the parents who had not responded one way or another, or simply not recalling that the study was still ongoing at the time of writing. In Bronner's thesis [MIT], it states that one of the boys did not participate in one of the tests because he was away on vacation. We can infer her answer to this requested change in plans was no.)

¹³F. Bronner, R.S. Harris, C.J. Maletskos, and C.E. Benda, "Studies in Calcium Metabolism. The Fate of Intravenously Injected Radiocalcium in Human Beings," *J Clin. Invest.* 35, 78-88 (1956).

July 1952-June 1953 (Appendix B-26)

Annual Report of the Research Laboratory/Fernald highlighting the calcium metabolism studies (on page 3). It verifies that studies using ^{45}Ca were still ongoing through this time period.

September 29, 1953 (Appendix B-27)

 Correspondence from Benda (F) to the AEC requesting permission to inject 50 uc (microcuries) of ^{45}Ca into "a moribund gargoyle" (an archaic and unacceptable term used at that time for persons with Hurler-Hunter syndrome) who was hospitalized at Fernald. This was a ten-year-old boy whose "life expectancy is now limited to a few months." It is noted that "permission for the use of higher doses administered to moribund patients has been granted by you to other investigators, as evidenced by the report of Sallin and Lasslo (*Science* 117, 331-4, 1953)."

(NOTE: This is the only record the Task Force found of the administration of a radioactive isotope to a terminally ill resident at this or any state-operated facility.)

October 6, 1953 (Appendix B-28)

Correspondence from Benda (F) to a parent noting that "we cannot find that we have ever received a reply to our letter of August 7 asking permission for your son to participate in examinations in connection with the nutritional department of the Massachusetts Institute of Technology." He states that the studies are designed "to improve the nutrition of our children." Benda also states that the young man in question has "expressed willingness" and asks that the permission slip be signed and returned.

December 2, 1953 (Appendix B-29)

Correspondence from Harris and Bronner (MIT) to Farrell (F) outlining plans for the Science Club members' Christmas party.

1955

October 18, 1955 (Appendix B-30)

A list of 37 boys, with a notation identifying parents/guardians to be contacted, or a designation of "no relatives," meaning they would be deemed "state wards." Thirty-three letters are noted as having been sent to parents for permission for the boys to participate in the study. (Note: The Task Force has not found any records relating to this last Calcium study proposal; therefore, it cannot be determined if the study was funded or carried out. However, the two Task Force members who were residents at Fernald and who have memories of being members of the Science Club did not live at the facility during the time of the earlier studies. As a result of their memories, the Task Force believes that another Calcium study or studies did occur and are actively seeking information.)

October 18, 1955 (Appendix B-31)

Correspondence from Benda to a parent/guardian following up on his request for permission for her son/ward to participate in "some planned research." He states that "most of the parents have given permission" and requests a reply. This letter has the approval line signed by Farrell (F). (Note: Again, this would relate to the study for which no archival records have been found.)

1956

June 1, 1956 (Appendix B-32)

Correspondence from Dr. Jack R. Ewalt, Commissioner of DMH at this time, to the Superintendent at Fernald requesting a listing of current research projects, to be submitted to the Governor and "certain members" of the legislature to support their budget request.

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As the records reveal, these studies were carried out openly, with permission from the appropriate state and federal agencies given oversight in that era. Outreach for permission was carefully documented, including all steps taken to secure it. The results of these studies were freely published in the scientific literature of the day. Despite these governmental approvals, the accepted level of permission outreach of the day, and the publication

of the research findings, four troubling themes pervade these findings:

- Full disclosure of all relevant information (specifically that radioactive materials would be used) was not given to the proposed research subjects' parent/guardian to assure informed consent;
- The apparent attraction of state-operated institutions as the location for research studies to be done due to the controlled environment;
- The use of a potentially coercive factor, even if not intended in that fashion, by way of a set of "rewards" that would be almost impossible for an institutionalized person to resist, was offered in opposition to the opportunity that was given to the boys to withdraw or refuse to cooperate as subjects; and
- The lack of affirmative action required for the actual granting of consent.

How Could It Have Happened?

The question "How could it have happened?" has been the topic of numerous articles, talk shows, and personal discussions since these research studies were disclosed at the end of 1993.

This section will only briefly highlight the factors that contributed to the atmosphere of permission for the studies which occurred in the state-operated facilities administered by the then-Department of Mental Health (now the Department of Mental Retardation) in the 1940s through the 1960s. These factors served as subtle contributors to the pervasive atmosphere of the time that influenced the behavior of all persons involved.

These influences include the following:

- The laws that surrounded the issues of guardianship for those committed as state wards; and
- The laws and policies of the day concerning informed consent for research studies.

The section concludes with some compelling first-person narratives. They were submitted to the Task Force by persons who were themselves residents or family members of residents who lived at the Fernald School during this era. These documents provide insight into the everyday life within an institutionalized setting as no other archival record could ever achieve.

☐ Background on Guardianship & State Wards from 1940 to 1960

The laws of guardianship can be traced through most of the legal systems in the civilized world. Dating back to Roman law, governments provided protection of property of individuals deemed to be incompetent. The legal principle, once established, flourished and became standardized in English law for persons who were mentally ill (as all persons who also had any form of cognitive disability, social or cultural issues, or mental retardation were once termed). Much of the law of the United States is deeply rooted in English law.

"Statutory provisions for the restraint and care of the mentally ill dates from the seventeenth century. In 1676, town selectmen [in Massachusetts] were charged with the care of distracted persons ... that are unruly, whereby not only the families wherein they are, but others, suffer much damage by them, so that they do not damnify others."¹⁴ In 1694, Massachusetts expanded the statute regarding the appointment of a guardian for persons deemed mentally disabled. The statute provided that municipal officers must "provide for the relief, support and safety of any person who is naturally wanting of understanding so as to be incapable to provide to him/herself or who shall fall into distraction and become non compos mentis."¹⁵

In 1726, the Commonwealth enacted the first statute pertaining to the appointment of private guardians for "any idiot [sic], non compos, lunatik [sic], or distracted person."¹⁶ The same statute provided for judicial determination of mental incompetence. The statutory standard that mandated the appointment of a guardian if an individual was found not capable of taking care of him/herself remained the prevailing standard for more than 150 years.

¹⁴*Doe v. Doe*, 377 Mass. 272-275 (1979) (citing 5 records of the Governor and Company of the Massachusetts Bay in New England 1674-1686, 80 [1854]).

¹⁵Cross et al., *Supra*, 1-10 (quoting Province Laws 1693-1694,c.18 §1).

¹⁶*Doe v. Doe*, 377 Mass. 272-275 (1979) (citing Province Laws 1726-1727,c.12 §1) .

The statutes pertaining to persons with mental illness were incorporated into the 1932 General Laws of Massachusetts, Chapters 123 and 201. Section 2 of Chapter 123 provides in part the state's role: "[The Commonwealth shall have] the care, control and treatment of all insane, feeble-minded persons...the care of whom is vested in it by law, and of each person who shall hereafter be received by any state hospital." Through this section, the Commonwealth of Massachusetts retained exclusive control over and custody of those deemed mentally ill.

Section 4 of Chapter 123 continues to outline the responsibilities of the Commonwealth by mandating that *"the commissioner shall administer the laws relative to persons in institutions under the general supervision of the department."* The Commissioner, or Superintendent of a particular facility, possessed great authority in the regulation of not only the affairs of the institution but also the affairs of the individuals within the institution. In addition, in Section 11 of Chapter 123 the statute directs the Department of Mental Diseases to *"encourage scientific investigation by the medical staffs of the various institutions,[and it] shall publish from time to time bulletins and reports of the scientific and clinical work done therein."*

Chapter 201 of the General Laws provided that a *"guardian of a minor shall have the custody of his person and the care of his education, except that the parents of the minor, jointly or the surviving parent, shall have such custody and said care unless the court otherwise orders."* The statute continues to define the rights of the guardian in Section 12, which provides that the guardian *"of an insane person ... shall have the care and custody of the person of his ward, except as provided in Section 24 [regarding married women] and the management of all his estate."* In a very real sense, the guardian took responsibility for the care and custody of the ward. In cases of a child whose parents or other family members were not involved, the superintendent became the guardian and the child was considered a *"ward of the state."*¹⁷

In Dr. Stanley Herr's book, *Rights and Advocacy for Retarded People*, there is a compelling quote that reflects the level of authority and power that was vested in an institution's administration when it came to day-to-day control it had over the residents' lives: *"Once an individual was committed, the legal system's role abruptly ceased. Rights were permanently abrogated by conditions that destroyed any expectation of claiming them. The rule of the superintendent substituted the rule of law. The courts, like the rest of society, expected the superintendent to act on behalf of residents. Institutions had practically full authority over every aspect of their residents' existence. With virtually nothing to fetter their discretion, institutional staff exercised powers over the individual unique in American life."*¹⁸

The Commonwealth has a traditional power and responsibility, under the doctrine of *parens patriae*, to care for and protect the "best interest" of the persons residing in its institutions. However, the definition of "best interest" was left in the hands of the Superintendent or Commissioner to define. In other words, the Superintendent had total control and authority over every aspect of an institutionalized resident's existence.

☐ The Development of Informed Consent

It was only during the twentieth century that the idea of providing information about procedures to patients and/or research subjects began to be considered important. The history of informed consent as it relates to the research studies from the 1940s to the 1960s can best be understood by dividing its development into two distinct periods: pre-World War II (up to 1945) and post-World War II (1946-1972). *The changes that occurred from 1972 to the present will be covered in the next section, "Could It Happen Today?"*

■ Pre-World War II (up to 1945)

Prior to World War II, the doctrine of informed consent began developing based on a judicial deference to individual autonomy and the belief that a person should not be forced to act against his or her will. For

¹⁷MGL c.201 §12 (1932).

¹⁸S. Herr, *Rights and Advocacy for Retarded People* (Lexington, Mass.: Lexington Book) 1983, p.9.

example, in 1914 Justice Benjamin Cardozo stated: *"Every human being of adult years and sound mind has the right to determine what shall be done with his own body."*¹⁹

Early consent doctrine was based on the common law tort of battery, defined broadly as an "unconsented to touching." Being based on the tort of battery, the idea of informed consent during this time period was, in fact, quite limited. For a physician to meet his/her duty under the law, s/he generally needed only to explain the procedure in general terms to the patient.²⁰ There was no common law requirement that the physician disclose to the patient the risks of the procedure, other treatment options, or any of the other substantive components of today's informed consent requirements. In addition, there was nothing in the law which specifically required that the patient actually understand what the physician was telling him/her. So long as the physician gave the required explanation to the patient, and the patient seemed to understand what was being told to him/her, the physician was held to have met the requirements under the common law consent doctrine of the time.

There was even less concern with informed consent prior to World War II from the statutory side of the law. To state it succinctly, there were no statutory and very few other formal codes for informed consent prior to 1946.

The pre-World War II law of informed consent with respect to children was based on the traditional view that children were legally unable to give consent. Based on the common law, the parents of the child, or his or her legal guardians, were the ones entitled to give consent for any procedures the child might undergo.²¹ In the case of *Bonner v. Moran* (125 F.2d 121[D.C. Cir., 1941]), a federal appellate court considered the question of consent by a minor and affirmed the general rule that the consent, either expressed or implied, of a parent/guardian is necessary for any operation on a child. The court did note that there were exceptions to the rule where there was an emergency, the child was emancipated, or the child was so close to maturity that the surgeon could rely on his/her own consent. However, in such cases, the procedures were for the benefit of the child whose consent was accepted.

■ Post-World War II (1946-1972)

The starting point for most discussions of informed consent is Nuremberg, Germany, at the trial of the Nazi doctors. From December 1946 through August 1947, twenty-three defendants were put on trial, charged with crimes against humanity. During those eight months, dozens of witnesses and over a thousand documents were presented, all of which told a story of the cruel and inhumane experiments conducted at the hands of Nazi doctors -- experiments in which unwilling subjects were tortured and ultimately killed in the name of research. At the conclusion of the trial, in which death sentences were imposed on seven of the defendants, the governing body created a set of ethical guidelines for future human experimentation. This set of guidelines became known as the Nuremberg Code (see Appendix H).

The first section of the Nuremberg Code states the following: *"The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. ... The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity."*

The tribunal that put forward the Nuremberg Code consisted of judges from the United States. Elements of the Nuremberg Code, including the informed consent requirement, became the framework for two new federal regulations that increased the rights of research subjects. During the late 1950s, the Clinical Center of the National Institutes of Health (NIH) adopted guidelines for research volunteers. The Food and Drug

¹⁹ *Schloendorff v. Society of New York Hospital*, 211 N.Y. 125, 105 N.E. 92 (1914).

²⁰ See Furrow et al., *Health Law* at 322.

²¹ For a discussion of the history of children in research, see Grodin & Glantz, *Children as Research Subjects: Science, Ethics & Law*, 1993.

Administration (FDA) also issued informed consent regulations, but only after the Kefauver-Harris Amendments to the Federal Food, Drug and Cosmetic Act of 1962 were enacted.

Both of the federal regulations, however, were limited in their applicability. The NIH regulations applied only to research that was conducted by researchers at the National Institutes. With the FDA regulations, sanctions for not obtaining consent were levied against drug sponsors, not individual physicians. Therefore, these guidelines provided little direct incentive to individual researchers to ensure that all research subjects were giving an informed consent.

Within the research community itself, the acceptance of the Nuremberg Code was less well received. In part this is due to the fact that researchers in the United States felt that the basis of the Nuremberg Code (i.e., the Nazi atrocities) were so unlikely to occur in this country that the Code might not be necessary. For example, one physician said, *"I think we must read the Nuremberg Code in reference to the conditions under which it was written. This is a wonderful document to say why war crimes were atrocities, but it is not a very good guide to clinical investigation which is done with high motives."*²²

In addition, there was concern that the Code was too legalistic and difficult to apply in actual research settings.¹⁰ Against this backdrop, the research community organized and developed a new set of ethical principles to guide researchers. Known as the Helsinki Declaration, it was adopted by the World Medical Association in 1964 (see Appendix H). The Helsinki Declaration is unlike the Nuremberg Code in that it clearly stresses the importance of research, stating that *"it is essential that the results of laboratory experiments be applied to human beings to further scientific knowledge and to help suffering humanity."* Developed by physicians for physicians, and explicitly recognizing the importance of research, it is not surprising that the Helsinki Declaration was greeted warmly by physicians in the United States as a preferable alternative to the Nuremberg Code.

Why then did research still occur in this time period that was in direct contradiction to the guidelines set forth in these documents? In part, the legal and political systems may be to blame. For all the initial talk of the importance of informed consent and the Nuremberg Code, not a single U.S. court even cited the Nuremberg Code until 1973, over 25 years later. In reviewing state common law, the Task Force found that even in Massachusetts, which has a history of being in the forefront of medical research, there was no judicial recognition of a right to informed consent until after 1982.

There were, however, precursors within the Massachusetts court system to the doctrine of informed consent.¹¹ A number of decisions in Massachusetts stressed a support for a broad, rather than a narrow, construction of the related issue of a physician's duty to disclose to a patient.¹² These cases indicated that the court system was leaning toward the right of the patient when it came to whether or not information should be given the patient by the physician.

During the years 1946-1972, there was little evolution of the law of informed consent as it applied specifically to children. As it was prior to these years, a child was generally deemed legally incompetent, and any decisions on being a research subject were left to his/her parent or guardian. The Helsinki Declaration specifically states that, *"Clinical research on a human being cannot be undertaken without his free consent [and] if he is legally incompetent, the consent of the legal guardian should be procured."*

²² P. Beeson, "Panel Discussion: Moral Issues in Clinical Research," *Yale Journal of Biology and Medicine* 36, p.464 (1964).

¹⁰ G.J. Annas and M.A. Grodin, *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation* (New York City: Oxford University Press), 1992 p.204.

¹¹ *Forner v. Koch* 272 Mich. 273, 261 N.W. 762 (1935); *Bonner v. Moran*, 125 F.2d 121 (D.C. Cir. 1941); and *Prince v. Massachusetts*, 321 U.S. 158, 170 (1944).

¹² *Madsen v. Harrison*, No. 68651 Eq. Mass. Sup. Jud. Ct., June 12, 1957; *Huskey v. Harrison*, No. 68666 Eq. Mass. Sup. Jud. Ct., Aug. 30, 1957; *Foster v. Harrison*, No. 68674 Eq. Mass. Sup. Jud. Ct., Nov. 20, 1957.

No federal or state regulations were promulgated dealing with children as research subjects until the 1970s, and any judicial cases during that time were decided on the basis of guardianship issues and not informed consent.

(Note: Additional research provided by two attorneys who were members of the Task Force on the issue of informed consent is in Appendix L.)

□ Narratives

Life was very different for residents in state-operated facilities and their families from the 1940s through the 1960s. Many residents were there because physicians and other "experts" advised parents or guardians that state schools were the only solution to the medical and social problems facing them. Superintendents exercised almost absolute authority. The threat to "send the resident home" was enough to dissuade most parents from asking too many questions or disputing school practices.

Until the 1970s, buildings were dirty and in disrepair, staff shortages were constant, brutality was often accepted, and programs were inadequate or nonexistent. There were no human rights committees or institutional review boards. If the Superintendent (in those days required to be a medical doctor) "cooperated" in an experiment and allowed residents to be subjects, few knew and no one protested. If nothing concerning the experiments appeared in the residents' medical records, if "request for consent" letters were less than forthright, or if no consent was obtained there was no one in a position of authority to halt or challenge such procedures. Hence, if the Superintendent failed in his duty to the residents, there were few if any witnesses or advocates available to safeguard the interests of the residents.

The following is a series of observations of life at the Fernald School during this period, written by those who lived it firsthand.

My Days at the Fernald School

by Charles L. Dyer

March 4, 1994

Looking back at my younger days during the years 1955 -1961 one would say I have a lot of mixed thoughts and emotions.

When I first entered the School I thought I was going there to learn and maybe better myself. But the days turned to months and the months turned to years with little understanding as to why I was there. As time went on, I guess I started to get bitter: not really having any freedom and finding out that it wasn't a school for learning, but in fact an institution for the mentally retarded. One can't help but ask ... why me?

I saw a lot of abuse going on while I was there. Not only to myself but to others as well. During one instance, I saw an employee burning a mentally retarded child with a lit cigarette.

My bitterness then turned to rebellion. I didn't care anymore, I just wanted out. To this day, I can't tolerate someone telling me what to do and when to do it. I believe I was misled not knowing right from wrong, I would agree to anything if it meant freedom (as I knew it). Getting out of the four walls that I felt held me captive. Upon my release from the School, I was put on parole. Now if that doesn't make a person feel like a prisoner then I don't know what does.

It's time that all those promises that were made years ago finally be kept today. My only hope is that times have changed for the better.

Austin LaRocque's Memories

March 8, 1994

Dear Rev. West:

You asked me to share my memories of having been a resident of Walter E. Fernald School back in the years 1950-1960. From the understanding I have gotten from the documents I've received from the Fernald State School, I was put into the school for my "best interest" in terms of the areas of learning and receiving an education, but unfortunately this did not happen -- and I hope that in the future such problems will never occur with other children.

Once I was committed into the school, I was put in a building called B.D. I had many difficulties while in this particular building for two years, such as trying to adjust to taking orders without getting into trouble and getting punished for stupid little things such as talking back to the attendant with your honest opinions. Therefore, this has made me very bitter toward the Institution. It also makes me feel no trust in anyone other than myself.

I was then informed that I had a sister Rose Marie LaRocque here at the Fernald State School and this did give me a lift up in life. This made things easier to accept because the school allowed me to visit with her occasionally. This helped to fill my feelings of rejection when other children had visitors and I didn't. I didn't feel quite as alone.

In approximately 1955 or 1956 I was transferred to B.H. This time I was offered the right to become a mail delivery person throughout the school and I accepted the job gladly because it gave me the opportunity to see my sister on a daily basis. And then the next opportunity came when someone came to ask us if we would like to join a "Science Club." Because of the need for independence and recognition, we would gladly join anything to receive a small token of appreciation.

Technically, I feel that this particular "Science Club" was very dishonest with the children that joined, mainly due to the fact that they did not explain to these children what they were going to do to them and what kind of future effect it would have on them. Therefore, I feel that they should be held accountable for all medical problems that have occurred to these children. Also, anyone else who was involved with this particular program - especially Malcolm J. Farrell who is just as responsible as anyone else because he agreed to the "Science Club" and allowed this program to occur. In my honest opinion I feel that he has done an injustice to all of these students. Only because, to the best of my knowledge, Malcolm J. Farrell was supposed to have medical knowledge and because of this I feel there's no excuse for his allowing it.

Dorothy Bourdon: Resident of Fernald since 1947

By Doris Manson

March 1994

In 1947, on the advice of my physician, I brought my daughter, Dorothy, to Fernald to be evaluated. She was then 5½ years old and had spoken a few words. Since she had ceased to speak, I was told she had regressed to a lower level of organization and probably would not now develop mentally beyond the age of a 5-year-old. They advised that she be admitted to Fernald.

Dorothy is non-verbal, and I doubt that she understood the spoken word at this time. She was constantly frustrated, banging her head on points of furniture, door knobs, etc. She would bite the backs of her hands until she drew blood and they became calloused. Many a day she would put her head through the windows and almost monthly had to be rushed to an emergency room for stitches. This behavior continued after she was admitted. I was at my wits end. I finally, on May 5, 1947, brought her to be admitted to the West Building of the Fernald School.

I was advised not to visit for 2 months or more, to give her a chance to become acclimated to her new surroundings and hopefully to wean her away from me. This never happened. The first Sunday of each month was the only time visiting was allowed. When I arrived, I was not allowed beyond the foyer. Dorothy was brought to me. I never saw where she ate or slept for many years.

On these visits, I would hold her and rock her the whole time, and when it was time to leave she would cling to me desperately, crying and sobbing until she was forcibly removed. Each month I would hope that maybe in another month I would find her happier.

When I look back on this period of my life, I wonder how I ever parted with my only child. I was convinced at the time that I was making the best decision for her, protecting her from the Community ills and providing a roof over her head with three meals a day in the event of my death. Since then I have questioned the fact that I was young and maybe trying to "get a life" as the kids would say today.

West Building is the oldest building on campus. It left much to be desired as far as living quarters and care. On visiting, I occasionally got a glimpse of the day room. It was a large, bare room with a cement-like floor. In the middle of the room there was a circular grating where urine and feces were hosed down. Needless to say, the little girls wore no panties. This room had no chairs, the children sat or laid down on the cold flooring. Most of the children laid on the floor because they were given Valium two and three times a day. Many a controversy I had with the doctor over Dorothy's dosage, to no avail.

I never saw the bedroom until much later. It was a very large, ward-like room with many beds only inches apart. The only shower I ever saw was on the back porch. The children were taken naked, outside in view of any passerby, to be showered. I am convinced this could not have been a warm shower. The dining area was one large room with long tables and benches. The children sat side by side and frequently stole food from each others' plates. One soon learned to eat fast.

Dorothy was so tranquilized that she could not defend herself. On two separate occasions she had the skin torn off both sides of her face, neck and back. No one could give me an explanation of what was happening to her, only that they found her all bloody each morning. I brought her home each time until she was completely healed and I was successful in getting her sleeping quarters changed.

She was moved upstairs. It was here I saw roaches, red ants and mice darting in and out to pick up a few crumbs left on the floor. My daughter was delighted with the mice. This building was ultimately condemned for living quarters and Dorothy was moved to West Kelly Building. It was about this time they decided to integrate the sexes; the ladies were housed on the top floor and had to go down three flights of stairs to each meal. The dining area was very large and very noisy and Dorothy was very nervous.

I saw children in Dorothy's area restrained in straight chairs and left alone in outside halls with all doors closed to them. There were no rules in place regarding restraints. The bathroom was one long row of stalls with no doors. There was no privacy. By the time many parents had banded together forming the Fernald League for Retarded Children. Subsequently, we were allowed to visit inside the buildings and I was now taking Dorothy home each weekend.

It was an experience getting in and out of this building. Dorothy would get very nervous when many of the men would get close to us and would strike out at them. Many a belt she received in return, before I could intervene. I had to be sure I always had a pocketful of nickels when I visited, otherwise the men milling around on the first floor would bar my way, or would not open the door for me. We also had to pass many men standing around masturbating inside and outside of this building.

Dorothy suffered a head wound in this building. Her skull was compressed over her left temple and she had several stitches. Again, no explanation was ever given to me. To my knowledge, she was not subject to seizures before this. Sometime after this injury she was placed on Dilantin, twice a day, for seizure activity. I was successful in getting her transferred again. This time she was placed in Withington.

Withington Building was always a mystery to me. I never could get beyond the Nurse's office. I do know my daughter was very unhappy here. Her next move was to Sequin Hall. By now the League was successful in

their "Class Action Suit" against the State and many changes took place. We were successful in implementing rules and regulations against restraints, injuries, abuse, etc. We also had toilet tissue in all bathrooms!

The League at this time bought many washing machines and televisions for the different buildings and financed their upkeep. We had programs in place for the children: many van trips for ice cream, to zoos and circuses, to see Christmas lights, etc. We had cookouts, family days, Halloween parties, spring balls and Christmas parties. We also had vacation trips to New Hampshire and the Cape.

At Sequin Hall we had many fine folks in place, a wonderful caring nurse, Ella Stephens, and many devoted Direct Care people. Dorothy seemed to be doing fine here, but then they decided Sequin had to be renovated, so once again, she was moved to the Woodside Building.

At the Woodside Building we had our very favorite, kind, wonderful nurse and many fine Direct Care people. In spite of all this, a rape occurred here involving a wheel-chair patient. Dorothy remained here quite happy, for nearly five years then she was transferred back to Sequin Hall.

As Building Representative for Sequin, I have worked very hard getting this building on line, mostly by complaining. Now that I am delighted with everyone and everything in Sequin, they have decided to move most of the clients to the Wallace Building.

I have been Building Representative for Wallace and never uncovered too many problems here. Many of the people who work here have been with Dorothy in the past. Since she has to move, I am pleased she will be at Wallace with many of her old friends.

I have left out many sad stories: the girl found at the bottom of the pool because someone neglected to take a head count; the girl who wandered out of her building and died in a culvert from hypothermia; the girl who received blows to the head from a male care-taker because she "smeared." This child finally stopped eating before anyone discovered her plight. When taken to M.G.H., she was diagnosed with infection from trauma to the head. When this man was confronted and told we had a witness to his abuse, he quickly disappeared and was never prosecuted. Could he be working in the community with our children today?

At this present time, we have a building being investigated due to 12 injuries reported in a year. These are all broken bones and it has not been determined yet if this is abuse or neglect -- or is it a case of more and better training needed for the care-takers of these fragile children?

I was hoping to go to "Glory" in peace, but I guess that is not to be.

Joanna Bezubka: Life & Times at Fernald

by George Mavridis

February 1994

This is a first-person history of Joanna Bezubka, a lady with Down syndrome. Joanna is a resident of the Walter E. Fernald State School.

Profile

Joanna was born May 15, 1951, four and a half years after her brother Ronald. Joanna was admitted to the Fernald State School in 1966 when her mother died during unsuccessful heart surgery. Joanna's father died in 1969 from Alzheimer's disease. Stella Mavridis, Joanna's maternal aunt, and Walter Bezubka, Joanna's paternal uncle, became co-guardians and I became a co-guardian when my mother died in 1991.

Joanna is severely to profoundly retarded. Today at age 43, her mental age is about two. When Joanna is humming, she is happy and feeling well. Joanna communicates by hand signals, coughing with tone inflections, facial expressions and one word requests. Joanna's speech is marked by mild dysfluencies which are displayed as short breaths, shaping and reshaping her lips and mild consonant repetitions. If you respond to the hand

signals or coughs, you may never realize Joanna can speak. I do not believe she knows technical family relations; when Joanna wants you she calls, "Maaa!" Joanna does not understand I am her maternal first cousin.

Early Years

The first memory of Joanna's care was her mother's concern during the first few months because Joanna was not developing like a normal child. Joanna did not sit up, crawl or show any other normal signs of growing. Joanna's mother and aunt took her to the doctor and were told for the first time that Joanna had severe to profound mental retardation. I assume the doctor knew Joanna had Down syndrome at her birth and withheld the information from Joanna's parents. No one ever explained why the doctor withheld this information for several months. He certainly did not expect the retardation to disappear. In 1951 the prognosis was that Joanna was profoundly retarded and would not attain the mental age of 2 until she was 12 to 14 years old and would not live past 20.

The next memory was the shock and disappointment of Joanna's grandparents when they learned about Joanna's retardation. How could my aunt destroy their son's family by giving him a retarded child? The paternal grandparents never offered to help care for Joanna. However, Joanna's Uncle Walter was the key person during the negotiations with Fernald in 1966 for Joanna's placement. From 1951 to 1966 we did not receive any services for a family with a mentally retarded child. I do not remember receiving any education in the care of a child with mental retardation. The doctor told us to keep Joanna at home as long as possible before placing her at Fernald. Our family knew placement was inevitable and tried to delay as long as possible, but my Aunt's pending heart surgery forced us to place Joanna in the Fernald.

Memories

In 1966, after my aunt's untimely death, Joanna's care became the responsibility of our grandmother, my parents and me. For personal reasons which are not relevant to this history, Joanna's brother, Ronald, and her father could not provide for Joanna's care.

I do not remember Joanna's reaction to her mother's death. Digressing a minute, I remember her reaction to my mother's death in 1991. The late Father Henry Marquardt, Fernald's Chaplain, and a nurse took Joanna aside and talked to her about my mother's sudden death. Joanna did not seem to listen until Father Henry said my mother had gone away and would not return. He said Auntie Stella still loved her and would always watch out for Joanna. Joanna sat up as Father Henry spoke and paid attention to his words, then she said, "All gone." The next weekend I asked Joanna, "Where is Auntie Stella?" Joanna responded, "All gone."

Prior to my mother's death I was the loving cousin Joanna wrapped around her little finger. Mother always said Joanna would be crushed if I ever raised my voice and reprimanded her. After my mother's death Joanna respected me as the final authority during home visits and never walked around the house looking for Auntie Stella. I never asked the question, "Where is Auntie Stella?" again. But I tell her how proud her mother, grandmother and aunt are, when Joanna is doing something well.

From 1966 through 1979 my grandmother lived with us and Joanna came home biweekly on Friday afternoon and stayed until Sunday. We took Joanna back for the evening meal. From 1979 through 1988 my parents and I continued the biweekly visits. Today I can not care for Joanna overnight, so I try to take her home every Saturday.

Fernald: The Early Years

In 1966, the Fernald policy was to isolate new residents for 2 or 3 months from their families. I do not know when this policy was stopped but I know it did not destroy Joanna's family memories and ties.

During the early years at Fernald, Joanna lived at Greene. I still remember the long walks down the long second floor corridor past barracks style rooms of people with mental retardation and Joanna's protests about walking to her room. The staff was always in their office on the first floor. No one asked how Joanna enjoyed her weekend at home or how was her health at this time. They just relaxed and continued their conversation. It was obvious they had no idea what was happening on the second floor. The staff at Greene demonstrated the expression "warehousing people with mental retardation" perfectly.

Joanna knew the weekend visit was over when we entered the Fernald campus and tried to prolong it. She refused to leave the car, walking up the stairs slowly and reluctantly. The return trips were very emotional for my mother. I never let my mother drive to Fernald alone because I knew she would not be able to drive home alone. Mother cried every Sunday night after returning Joanna to Fernald.

Consent Decree

Six years later the parents sued the Commonwealth in federal court and life for Joanna and the other residents in all the state schools plus those in community facilities started to improve. The first renovated building Joanna called home was a cottage, the next was Warren Hall and today she lives in MacDougall Hall. Joanna moved into MacDougall just before her scoliosis operation. The ladies' apartment is on the first floor. Joanna's first day program was at an unused school in Woburn. Today Joanna's day program is in the renovated Manual Building. The increased staffing allowed Joanna to enjoy finger painting for a few years, to learn some routine chores like folding clothes in the laundry, and clearing dishes from the table after meals. She uses food utensils better and is more relaxed. The return trips to Fernald are not as emotional as they were in the early years.

Medical Care

My first bad memory of Joanna's medical care was a call from the dentist who extracted all her teeth so Joanna would not be bothered with tooth decay and cavities. Her mother always took Joanna to a dentist and her teeth were excellent in 1966. One or two years later a Fernald dentist extracted all Joanna's teeth for Fernald's convenience. I know my mother did not give any consent and definitely not "informed consent" for the extractions. Since the extractions Joanna must eat pureed or ground food. She can not enjoy chewing a good piece of meat. The next bad memory was the poor sanitary conditions of Fernald in the early years. Joanna walked on dirty bathroom floors and all her toe nails are deformed. Her toe nails must be cut by a podiatrist.

The good memory was a call from Dr. Goldberg of the New England Medical Hospital in 1987. Dr. Goldberg had been monitoring Joanna's scoliosis for several years. Joanna's medical record has a letter which noted her scoliosis was getting worse, but Harrington Rod operations were too difficult for Joanna. The letter was written in the late 1960s. In 1987 technology had improved so Dr. Goldberg proposed two 8-hour operations to straighten Joanna's back. The operations were done in the spring of 1988. The first operation straightened her back 55 degrees and fused all the disks. The second operation two weeks later inserted a Harrington Rod and Lukey Rod to reinforce her backbone. Post-operation recuperation lasted six months. Three months were spent in the Fernald acute care clinic lying on a Baxter Frame. I can not say enough good words about the direct care staff who monitored her hospitalization in Boston, the Fernald medical staff and the New England Medical Center staff. We visited Joanna every day for six months and observed the staff during all possible situations. My favorite memory was the week a young man was in the New England Medical Center for a similar operation. We agreed to place him in Joanna's room so one Fernald employee could monitor both patients. Department of Mental Retardation social engineers quote privacy regulations; parents use common sense providing services for the individuals. The operations were 100% successful. Joanna's internal organs hang properly and she has not had bronchial illness or regurgitation problems caused by her hiatal hernia since the operation. She can sit upright in a chair, and walks without holding a wall. Dr. Goldberg told my mother and me that authorizing a scoliosis operation for a third person requires at least six months of evaluation. He told us to talk with the Fernald doctors and nurses who would monitor Joanna's recuperation. He was correct. Playing God for a severely retarded person was the most difficult decision mother and I ever made. I will never forget Joanna's eyes; they asked, "Why did you allow this to happen?" after each operation.

Post-Consent Decree

Today, it has been 2 years since my mother died. Joanna comes home 9 out of 10 Saturdays. I pick her up after breakfast and bring her back in time for the evening meal. An average day is playing with Lego toys, eating out my refrigerator and going for a ride. Joanna is very bright. I wish she could have been born 30 years later to take advantage of the improvements in services provided people with mental retardation.

One day an advocate remarked, "Oh, what we don't do for the Fernald." My mother answered quickly, "We do nothing for the Fernald, everything is done for the children." "We do nothing for the Fernald, everything is done for the children" is now my motto. Advocates must never take these improvements for granted. The Commonwealth of Massachusetts does nothing voluntarily for people with mental retardation.

Could It Happen Today?

■ Federal Laws of Protection

In the late 1970s major changes began to occur in the protection of human subjects in medical research. In 1974, the federal government adopted a set of regulations specifically addressing the protection of human subjects in experiments.¹³ During that same year, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research was created and given the chore of identifying basic ethical principles for human subjects.

These ethical guidelines, which were officially adopted in August 1975, require any institution that receives research funding from the U.S. Department of Health, Education, and Welfare to establish an institutional review board (IRB) to review and approve any prospective research involving human subjects. Furthermore, the IRB must be comprised of individuals from varying backgrounds, including a "lay member" from the public. The concept of the lay member was to ensure some type of public scrutiny over the IRB as a safety measure.

Under this law, if a research subject is to be placed at risk, as defined in the regulations, then the subject or his/her legally authorized representative must give informed consent, defined as the *"knowing consent of an individual or his or her legally authorized representative, so situated as to be able to exercise free power of choice without undue inducement or any element of force, fraud, deceit, duress, or other form of constraint or coercion."*

Unlike earlier ethical guidelines, such as the Nuremberg Code, these regulations place more emphasis on the rights of research subjects as opposed to their welfare, suggesting the general change from a paternalistic view of subjects to a freedom of choice view. Also, unlike the Code, the regulations allow for a legal representative to make an informed consent for another. This is true, in part, because the regulations deal with both nonbeneficial (nontherapeutic) and beneficial (therapeutic) types of research, while the Code dealt with nonbeneficial research only.

For beneficial research, the government did not want to expressly prevent a parent/guardian from consenting to a procedure that could save a child's life. Therefore, both types of research were lumped together with a legal representative having authority to consent to either.

Since 1974, federal regulations have been adopted that specifically address the issue of children as research subjects.¹⁴ These regulations apply to all research in any institution that receives federal funding for even one human research project.

The law defines "children" as persons who have not attained the legal age for consent to treatments or procedures involved in research, under the applicable law of the jurisdiction in which the research will be conducted. Therefore, if a state statute grants a child the right to consent at a certain age, or if the state judiciary has recognized the mature minor rule, these child regulations would not apply, and the general IRB regulations would be used.

¹³39 Fed. Reg. 18914 (May 30, 1974) (Covered all human subjects involved in research funded by the Dept. of Health, Ed., & Welfare. The coverage of these regulations has since been expanded.)

¹⁴48 Fed. Reg. 9818 (1983) .

The federal regulations for research on children adopt a four-category sliding scale system to determine what assurances are needed based on the type of research being conducted. The following research categories are:

1. Minimal risk to child, with or without a direct benefit to him/her,
2. Greater than minimal risk and direct benefit to the child,
3. Greater than minimal risk and no direct benefit to the child, and
4. A catch-all provision for any other research that doesn't fall into the other three categories.

For any of these categories, the regulations require that provisions must be made for soliciting the assent of the child and the permission of the parent/guardian. With respect to parent/guardian permission, the regulation states that for minimal risk, or risk with direct benefit research (i.e., category 1 or 2), the permission of one parent may be sufficient. However, for research involving risk and no direct benefit to the child, the regulation requires that both parents must give their permission, unless one is deceased or otherwise unavailable, or if only one parent has legal custody.

The regulations also provide special requirements for research on children who are wards of the state. There is an outright ban on any research with these children for procedures involving greater than minimal risk and no direct benefit (i.e., category 3 as well as category 4 research). In order to use these children in minimal risk research, or risk with direct benefit research, the IRB for the institution must appoint a child advocate to represent the child, in addition to any guardian or *in loco parentis*. The advocate must act in the best interests of the child.

As stated above, this regulation requires that provisions be made for soliciting the assent of the child, in addition to the permission of the parent/guardian. The term assent was used to separate it from legal consent, which, under some state laws, a child is unable to give. The job of determining adequate provisions for obtaining assent falls on the IRB. It must make an initial determination as to whether or not the child is capable of giving assent based on factors such as age, maturity, and psychological state. This must be done for all the children involved in the research protocol as a group or for each child individually. The regulations are clear that assent is not a requirement for no risk or risk with benefit to child procedures, although it should still be sought. Similarly, if the IRB determines that the children are incapable of assent, the assent requirement can be waived and the protocol can continue without their assent.

■ Department of Mental Retardation Regulations

Protection is also afforded individuals who are contemplated to be subjects in a research study by a set of regulations issued by the Department of Mental Health and the Department of Mental Retardation. Research activity is specifically regulated by 104 C.M.R. 13.00. The regulations codify requirements for advisory boards at the state level. The regulations also set forth additional standards of review, including, among others, the following considerations for inclusion:

- The subject's rights to health and physical safety;
- The right to confidentiality and privacy;
- The right to humane care and dignity;
- The right to self-determination and freedom of choice;
- The right to adequate care and treatment;
- The right to be free of undue discomfort, distress, and deprivation;
- The right to fair and equal treatment without discrimination; and
- Any other rights of clients that may be relevant to the particular project.

These regulations are currently being revised. The "Findings & Recommendations" section of this report includes specific recommendations for improving the language for increased protection for all citizens with cognitive disabilities.

■ The Role of Advocacy

During the 1950s and 1960s, mental retardation facilities such as the Fernald and Wrentham Schools were home for individuals who were referred there or committed to their care for a variety of reasons besides mental retardation. Many were placed there by the courts or by state social protection agencies. By the end of the 1960s and early 1970s these facilities had become so overcrowded that they served as little more than human warehouses.

Parents and other family members dissatisfied with these deplorable conditions founded parent associations to advocate for improvements in the care of the individuals living in each of these facilities. Belchertown Friends Association (now Advocacy Network), Dever Association, Fernald League, Parents and Friends of Monson, Wrentham Association, and Massachusetts Association for Retarded Citizens (now ARC Massachusetts) were all formed in the 1950s.

In the early 1970s, these parent associations poured their money, their hearts, and their talents into a collective pool and filed five lawsuits in federal court against the Commonwealth of Massachusetts and each of the five state schools because of inhumane, constitutionally unacceptable conditions that existed at the state schools. All these cases were settled by court orders known as consent decrees, which included agreements for an improvement in services and living conditions. There have been many improvements in the care given to individuals with mental retardation since that time, leading to the withdrawal of court oversight of mental retardation services in 1993. Each of these groups continues their advocacy efforts today.

In addition, many other advocacy groups have now been formed to protect the rights and dignity of individuals with mental retardation living in Massachusetts. Another parents' association, the Hogan/Berry Association, was formed in the 1970s. The 1980s saw the beginning of other new groups such as the Massachusetts Coalition of Families & Advocates for the Retarded (COFAR) and Voice of the Retarded (VOR). COFAR and VOR coordinate advocacy on the state and federal levels for the Dever Association, Fernald League, Hogan/Berry Association, Parents and Friends of Monson, and Wrentham Association. The Massachusetts Down Syndrome Congress (a group of parents and professionals concerned with the well being of younger children with Down syndrome) and local family empowerment organizations were also founded in this decade.

State and federal governments have instituted protection and advocacy groups such as the Disability Law Center and the Massachusetts Developmental Disabilities Council. Two university-affiliated programs at the Shriver Center and Children's Hospital also exist for the advancement in understanding causes of mental retardation as well as for the protection and well being of individuals with mental retardation.

The Department of Mental Retardation (DMR) has also been required by statute to establish a system of citizen advisory boards at all levels of the department to advise and review DMR policies and practices. Presently there are 29 such boards, involving over 400 citizen advocates. Human rights committees are required of every DMR program or facility to ensure protection. Everyone's desire to provide the least restrictive living conditions for individuals with mental retardation has stopped the commitment of individuals by the courts, state authorities, or their parents without due process.

The 1990s are witnessing the beginnings of effective self-advocacy, where consumers of state services are speaking for themselves in the shaping of policy and support services. These advocates have not only been the stimulus for dramatic improvements in services to individuals with mental retardation, but they have also served as a potent force to help prevent future abuses so common in the past.

Advocacy organizations are the vital link between the development and implementation of laws and other public policies created to protect vulnerable populations. There can be a vast difference between getting legislation written or passed and actually having it implemented properly to positively impact people's daily lives.

The most effective advocates at this level are the consumers and their significant others. No one can portray a need or issue as honestly and effectively as the ones who are actually dealing with it on behalf of themselves or someone they love.

Findings & Recommendations

FINDINGS (NOT PRIORITIZED)

I. The research conducted on human subjects at or from the state schools between 1943 and 1973 that involved the introduction of radioactive substances into their bodies was conducted in violation of the fundamental human rights of the subjects involved in that:

- The researchers failed to satisfactorily inform the subjects and their families that the nutritional research studies were non-therapeutic; that is, that the research studies were never intended to benefit the human subjects as individuals but were solely intended to enhance the body of scientific knowledge concerning nutrition;
- The letter in which consent from family members was requested, which was drafted by the former Fernald superintendent, failed to provide information that was reasonably necessary for an informed decision to be made;
- The researchers delegated the task of obtaining consent to the Fernald superintendent, and failed to ensure that proper informed consent was obtained from family members on behalf of the research subjects
- The provision of special rewards and privileges that were otherwise unavailable to individuals confined in an institutionalized setting, and otherwise unavailable to any other person residing in that institution other than those who were members of the "Science Club", resulted in the research subjects being unfairly enticed by those conducting the research;
- The Atomic Energy Commission allowed the researchers to conduct more than one invasive technique on any subject deemed "mentally deficient", while it limited such techniques to only one with subjects deemed to be of "normal" intelligence, even though it maintained the same maximum dosage for both subject groups; and
- The researchers administered a dosage of radioactive calcium (1.7 microcuries) that was in excess of the maximum dosage authorized at the time of the original licensing (1.0 microcuries).

II. The Commonwealth of Massachusetts, which was at the time charged with the responsibility of caring for the individuals in its custody, failed to provide basic protection to the individuals who were subjected to the research described in I above, in violation of their humans rights, in that:

- The superintendent's dual capacity in having the authority both to provide consent on behalf of state wards as well as to plan or approve medical research that would involve those same wards, seriously jeopardized the wards' right to protection and safeguard from harm;
- The researchers and facility staff at both Fernald and Wrentham failed to properly enter any information into the permanent medical records of the research subjects. This prevented any knowledge of the research studies to be passed on to future staff, thereby frustrating attempts to study potential long term issues.

III. Laws designed to protect persons with mental retardation from being subjected to experimentation are inadequate and need to be strengthened, to include:

- Current laws still permit non-therapeutic experimental research on individuals who are unable to give informed consent on behalf of themselves; and
- Current Department of Mental Retardation (DMR) regulations do not adequately protect individuals who are unable to give informed consent on behalf of themselves from non-therapeutic experimental research.

IV. In the best judgement of the experts whose opinions were sought by the Task Force, no significant health effects were incurred by the research subjects as a direct result of the nutritional research studies in which radioactive calcium and iron tracers were used.

V. The Thyroid study and the so-called Cold-war experiment, conducted at Wrentham, that utilized radioactive iodine, do present, in the expert opinion provided to the Task Force, the need for an immediate in-depth study to determine the nature and degree of any possible health risk. In these studies, no requests for consent have been located to date. As a result, a DMR working group, reporting directly to the Commissioner, shall continue the analysis on these studies.

RECOMMENDATIONS (Not prioritized)

1. All participants who were involved in human subject research which utilized radioactive materials at Massachusetts operated facilities for persons with mental retardation should be compensated for any and all damage incurred as a result of such research.

2. Participants, both positively identified and those the Task Force has significant reason to believe were involved as subjects, shall be entitled to federal benefits for any and all related health-care assessment and follow-up care indicated. The Task Force shall forward a recommendation to the appropriate federal agency requesting that a special fund be established. This fund shall be used exclusively to pay medical benefits for persons involved with these identified studies. At the very minimum, the persons shall be eligible for automatic medical benefits that shall include an annual examination, laboratory studies or other testing deemed appropriate.

3. DMR and this Task Force shall support the passage of "An Act To Require The Informed Consent of Human Subjects as a Condition of Performing Research Involving the Commonwealth's Facilities, Services or Funds". This legislation was filed on February 24, 1994, by Governor William Weld and given an original tracking number of as H4609 (copy in Appendix H).

4. The DMR's proposed new regulations (copy in Appendix K) on the protection of human subjects in medical research that are currently being revised and recodified shall be revised as follows:

- Section 10.03 (1):
delete in its entirety

- Section 10.07 (2)h:
add: After the experiment is fully explained, the subject or her/his guardian must be given a reasonable period of time to contact other experts and discuss the proposed research before he/she is asked to sign the consent form.

5. In fulfilling the Task Force's motion of a "duty to inform", DMR shall be charged with formulating and implementing a plan to provide information, referral, and advocacy for potential and identified subjects to address the concerns raised in the Recommendation section of the Final Report submitted by the Contact with Subject Subcommittee (copy in Appendix E).

- Former residents of the Fernald School (or their family members) who have called the "800" number, and whom the Task Force now believes did not participate in any of the major studies, are currently being sent a letter notifying and reassuring them that they were not a part of the identified research studies;

- All known subjects of the research studies shall be so notified orally and in writing within 30 days of the release of this report. As soon as all identified subjects have been notified, they, and others for whom there is concern, shall be invited to a "reunion gathering" at the Fernald School, or another location preferred by the participants. The purpose of this gathering would be to facilitate communication in a supportive atmosphere to allow peer support, contact with Fernald Social Work staff, as well as aid in the locating of other participants/former residents.
- The initial communication should take place in person, or if a face-to-face contact is not possible, it should be done by way of a carefully designed telephone conversation to be made by well-trained and prepared social work staff. A set of written materials should be provided concurrently;
- To facilitate ongoing communication with experiment participants, a "sole correspondent" should be identified for each person (preferably the same person who did the initial communication). This individual should have ongoing access to up-to-date information about risks as well as available resources for health and mental health services. Toll-free access should be maintained;
- For persons without access to mental health services, DMR shall identify options for counseling, including, but not limited to, personnel from the Department of Mental Health;
- If an experiment participant does not have health insurance, the Commonwealth shall provide assistance to facilitate linkage with an existing resource for medical care coverage (e.g. MassHealth) for services reasonably believed to be related to the research which utilized radioactive materials. If it is not possible to access financial coverage through traditional channels, the Commonwealth shall arrange access to and payment for such health care services;
- A packet of information shall be developed for research study participants to share with their physicians. This material shall include information pertaining to radiation exposure and potential implications for health-care; and
- A program similar to that set out above shall also be placed in effect for the Wrentham School subjects.

6. Any research done at a state-operated facility shall require the following information as part of the application process:

- the location for storage of the records after the completion of the study must be specified on the research study application;
- a percentage of the funds shall be earmarked for proper storage and professional cataloging of this information;
- any subjects must be named and noted with current address and social security number; and.
- a copy of the protocol and specifics of the study shall be put into the person's permanent file at any institutionalized setting and copy sent to their attending physician and the person themselves or parent/guardian, if applicable.

7. A document shall be placed in the permanent DMR record of each identified subject of any study, past, present or future. This will include a summary of the study and a notation of that individual's specific

involvement and drugs/materials used or received as is possible to ascertain. A copy shall be sent to their parent or guardian, if applicable. A special marking, identifiable only to DMR personnel on the medical staff, in medical records and in the social service departments, shall be made on the inside face sheet to indicate that this individual was a subject in a study. This will alert DMR personnel using that record to understand that special handling may be required if there is a request for a copy of the record. A referral will be made to the Social Services department for personal follow-up on that individual's behalf, in accordance with the standards set out in this report for contact with an identified subject. If that person has not yet been made aware of her/his involvement due to lack of a contacting address, a notation to that effect be made in their file as well.

8. Long term follow-up epidemiological studies shall be coordinated by the DMR working group, cooperation with the Department of Public Health, as recommended by the Working Group following the completion of its analysis..

9. The DMR Research Committee whose role it is to assure that proper procedures and follow-up is done all current or future studies, should have a minimum of 3 parents or significant others of current or former residents, and a minimum of 3 former consumers or consumer advocates on the board with a rotation of their term to be no more than 3 years. A request for suggested names shall be directed to the consumer organizations.

10. The Department of Mental Retardation (DMR) shall work in concert with the President's Inter-Agency Work Group commissioned to continue the investigation at the federal level. DMR, working with Senator Kennedy and Congressman Markey, shall request an official linkage with it by the naming of a member to as an official liaison. Further it will be requested that a member be named to the National Commission on Biomedical Ethics that is being recommended for formation by Senator Kennedy and Representative Markey.

11. The findings, archival and research materials from the work of the Task Force shall be placed into a permanent study section of the Howe Library. There shall be a request made to the Federal Interagency Work Group and the Presidential Commission to have a copy of their primary findings and records as well to create a comprehensive area for future study in the Howe Library on the topic of research utilizing radioactive materials with human subjects.

Appendix

- A. *Listing of Task Force & Advisory Group Members*
 - B. *Archival Record Chronology*
 - C. *Information Request Subcommittee*
 - D. *Methodology Subcommittee*
 - E. *Contact with Subjects Subcommittee*
 - F. *Introduction to Radioactivity & Radiation Primer*
 - G. *Expert Opinions: Radiation Dosimetry & Epidemiology*
 - H. *Nuremberg Code & Declaration of Helsinki*
 - I. *Governor Weld's Proposed Legislation*
 - J. *Consumer Organization List*
 - K. *Department of Mental Retardation Research Regulations*
 - L. *White-Lief & Tisei Research on Informed Consent*
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TASK FORCE MEMBERS

DR. MARY LOUISE BUYSE, M.D., M.S., graduated from the Medical College of Pennsylvania, Philadelphia in 1970. She is currently Medical Director at the Fernald State School. She has appointments at Massachusetts General and Newton-Wellesley Hospitals. Her specialty is in Pediatrics, Medical Genetics and Birth Defects. Dr. Buyse has extensively published with many articles focusing on birth defects and is the Editor-in-Chief of The Birth Defects Encyclopedia. She brings over 20 years of experience in developmental disabilities and medical knowledge to the Task Force.

DR. ALLEN CROCKER, M.D., attended Massachusetts Institute of Technology and Harvard Medical School, with training in pediatrics at the Children's Hospital. He has been associated with Children's Hospital for over 40 years. He has either written or contributed to over 100 articles and books. He teaches at Children's Hospital, Harvard Medical School and Harvard School of Public Health. He continues his long career at Children's Hospital with a focus on Developmental Disabilities.

DR. GUNNAR DYBWAD received his J.D. from the Faculty of Laws, University of Halle, Germany, and is a graduate of the New York School of Social Work. He is currently Professor Emeritus of Human Development at the Heller School, Brandeis University and senior staff member of the Center on Human Policy, Syracuse University, New York. Dr. Dybwad was consultant to President Kennedy's Special Assistant on Mental Retardation. He has a life long history of devotion to the betterment of the lives of individuals with mental retardation. He is known the world over for both his and his wife's (Rosemary) efforts in the field of developmental disabilities.

CHARLES DYER is a former member of the Fernald School's Science Club who now resides in Salem, MA. Mr. Dyer is a divorced father of three children: Danny, 28; Kelly Ann, 23; and Crystal Lee, 19. Danny suffers from the same problem as his father, which is small lumps appearing all over his body (doctors have yet to explain this condition). Kelley Ann was born with reversed organs (her heart and arteries are on her right side) and Crystal Lee was born with a hole in her lung which left her with asthma and breathing problems. Mr. Dyer was a truck driver for a produce company until 1992 when he was forced to leave due to an injury to his back while working. To take up his spare time, Mr. Dyer enjoys bowling, restoring and refinishing old furniture and collecting antique cars.

DR. ANNE HOWARD received her masters degree in Special Education, Severe Special Needs at Boston College and her Ph.D. in Social Policy (Developmental Disabilities) at the Heller Graduate School for Advanced Studies in Social Welfare, Brandeis University. Presently, she teaches special education courses at Fitchburg State College. She also provides consultant services to various public schools in regard to their special education programs and has written numerous articles in the area of health needs for persons with developmental disabilities. Dr. Howard is a member of the DMR Statewide Advisory Council (SAC).

RICHARD KRANT is a retired Special Agent of the Federal Bureau of Investigations and a member of the New York State Bar, Past President of Coalition of Families and Advocates for the Retarded (COFAR). In addition, he is a member of the Human Rights Committee at Wrentham State School, a member of the Advisory Committee to the Division of Investigations at DMR and a member of the Newton/South Norfolk Advisory Board. He is the COFAR representative to the Task Force. His son Bryan is a resident of Wrentham State School.

AUSTIN LAROCQUE is a former member of the Fernald School's Science Club who has resided comfortably, cozy and reasonably in Beverly, MA for 27 years. Mrs. Larocque, wife of 31 years, is a home health aide and mother and a loving companion to Austin. Together they have three children: Leo, 26, married for six years; Michelle Jane Anderson, 30, married for ten years; and Michael, 16, a sophomore at Beverly High School. Mr. Larocque also has a grandson, Bryan, 3, and a granddaughter, Kayla Ann, 2. Mr. Larocque's special interests and hobbies include playing pool and darts with his older sisters and long-time friend Charlie Dyer. Mr. Larocque has been a professional house painter for 30 years and currently holds the title of Janitor, Custodian and Painter for several Beverly area tenant buildings.

DORIS MANSON is a parent of a daughter living at the Fernald State School since 1947. She has been a member of the Fernald League for Retarded Children for 47 years. In addition, she has served as a member on the Fernald League Building Representative Committee, the Fernald Advisory Board and other ad hoc committees set up by the Fernald Administration. Ms. Manson accomplished her many goals at Fernald while working for 18 years at the Massachusetts Registry of Motor Vehicles in Boston where she has since retired.

REPRESENTATIVE EDWARD J. MARKEY has been a member of the Massachusetts delegation since 1976. Prior to that, he served two terms in the Massachusetts State House. In 1986, Representative Markey prepared and released the report entitled "American Nuclear Guinea Pigs", detailing 31 questionable radiation experiments on humans. He is also author of the book *Nuclear Peril* and a longtime advocate of a comprehensive nuclear test ban. More recently, he authored the Cable Consumer Protection and Competition Act of 1992 and has fought to reduce violence on the air waves.

GEORGE MAVRIDIS, P.E. has spent his career being a structural engineer, but has spent his life being an advocate for individuals with mental retardation. He is guardian to his cousin who is a resident at Fernald School and is President of the Fernald League for Retarded Children, Inc. Additionally, he is Vice-President of the Massachusetts Coalition of Families and Advocates for the Retarded. He also serves on DMR's Division of Investigation Advisory Committee, Mission Statement Committee and Fernald School's Human Rights Committee and Fernald League's Building Representative Committee.

FREDERICK M. MISILO, JR., (Chairperson) is the Deputy Commissioner of the Department of Mental Retardation. He possesses over seventeen years of combined experience in the field of mental Retardation and in private law practice. He holds a law degree from Suffolk University, a Ed.M. in Social Policy from Harvard University, and a B.A. from the University of Massachusetts at Amherst. Mr. Misilo is admitted to practice law in the Massachusetts and federal courts. He is also a member of the Health Law Section Council of the

Massachusetts Bar Association.

REV. DR. RICHARD J. ROBISON, D.Min. is the Director of Community Relations for the Department of Mental Retardation. He is the liaison for the Commissioner to advocacy and parent groups, statewide regional and area advisory boards. Prior to that he served as Protestant chaplain at the Fernald School. Dr. Robison is an ordained minister for the American Baptist Churches, USA. He graduated with a BA from Northern Illinois University, received his Masters of Divinity and Doctor of Ministry at Eastern Baptist Theological Seminary in Philadelphia, PA. Dr. Robison is the parent of three children, two with Down syndrome. He is also a board member of Mass. Down Syndrome Congress.

VIRGINIA TISEL, ESQ. is a sibling of a family member with developmental disabilities and has spent over 20 years advocating for persons with developmental disabilities. She is immediate past President of the Mass. Association for Retarded Citizens, a past President of the Greater Boston Association for Retarded Citizens (and a current Board Member), and has served on a number of task forces and committees for several years advocating for persons with disabilities. She is Asst. Labor Counsel at Grace Corp. in Lexington and is a former Special Assistant Corp. Counsel for the City of Boston. She is also a former educator in the Boston Public Schools.

DOE WEST (Project Coordinator) is currently completing her dissertation for her doctoral degree from the Law, Policy and Society Department at Northeastern University. Her MS in Rehabilitation Counseling is from Boston University and her M.Div. from Logos Bible College. She is a certified teacher of the speech and hearing handicapped, has served as a marriage and family counselor and lectured for the past 10 years at Northeastern University and Mass Bay Community College. She has spent over 21 years as a civil rights activist within the disability rights movement and was appointed the first Commissioner of Handicapped Affairs for the City of Boston, and created a national prototype office for Section 504 compliance within the Department of Health and Hospitals. A 1993 nominee to the Who's Who of Emerging National Leaders, Rev. West's most recent positions prior to the project included serving as Chief of Staff for a Massachusetts Senator and serving as a Chaplain for local hospitals.

DAVID W. WHITE-LIEF is a director of the law firm of Breakstone, White-Lief & Gluck, P.C. He graduated from the University of Vermont and received his law degree from Northeastern University School of Law. His areas of practice include (but not limited to) plaintiff's personal injury, medical malpractice, product liability and other civil litigation. He is the chair of the Human Rights Committee at the Fernald State School.

ADVISORY AND SUPPORT GROUP MEMBERS

DALE ANDERSON is Division Director at the Fernald School. Prior to that position, he was Human Rights Officer at Fernald. His responsibilities include developing programs and creating an environment at Fernald where residents and staff can maximize their learning and social interactions.

PAUL BIRMINGHAM is the Director of Campus Safety and Chief Investigator at the Fernald School. He also served as Human Rights Officer at Fernald. Presently, he is responsible for investigating complaints and reviewing reports of investigation in addition to overseeing the campus police and life safety.

KEN CAMPBELL is the Director of the News Office at Massachusetts Institute of Technology. A graduate of Yale University, he has been a reporter in Washington and London as well as for the *Boston Globe*. He has served as spokesman for the Boston transit system.

MARGARET DALE graduated from Boston University School of Law in 1976. She is an Associate Dean at Harvard Medical School and Director of the Office for Research Issues. Dean Dale served a vital role in her linkage and liaison to the personnel and resources of Harvard University. Her untiring commitment and perseverance allowed the work of the Task Force to be factually based and professionally finished.

REV. PAUL L. DUHAMEL graduated from Albright College and Andover Newton Theological School. He was director of Constituent Relations at the Fernald State School. Rev. Duhamel supervised the development of the first archival, research and client library for Fernald staff, residents and the public.

JOSEPH P. FOLEY, Jr. is currently a Clinical Social Work Supervisor at Fernald School and has worked for DMR for over 15 years at both the Fernald and Dever State Schools. He has a BA in Psychology, an MSW from Boston College School of Social Work and will complete the requirements for a Master's in Public Administration in May, 1994.

LINDA GERSHMAN received her BA from the University of Wisconsin and her Masters degree in social work from Boston University. She has worked as a clinical social worker at Wrentham State School since 1983 and has prior experience in the area of geriatric social work.

SENATOR EDWARD M. KENNEDY has served Massachusetts for 30 years as its Senator. His many contributions to his more vulnerable constituents are well documented, including legislation such as Civil Rights for the Handicapped, Comprehensive Child Development Centers, Long-Term Care for the Elderly and Disabled, the ADA, and many other health-related issues.

REPRESENTATIVE JOSEPH P. KENNEDY II was elected to the 8th Congressional District in 1986 and is serving his forth term. Serving on the Banking and Veterans Affairs Committees he has pushed through legislation opening up credit to working class families and people of color and has fought hard for the health-care needs of veterans. His concern for human rights has taken him around the world to places like Northern Ireland, Haiti, Germany, and Armenia.

KIRSTEN E. KENNETTE has, for the past 22 years, worked with clients at the Fernald State School in various capacities including direct care, training, and program management.

KEVIN W. KIRBY is working in the Investigations Department at DMR while completing his law degree at Suffolk University Law School. He also volunteers time as a special educational advocate.

DR. LOUIS LASAGNA graduated from the College of Physicians and Surgeons at Columbia University in 1947. He is Acting Chairman of the Department of Pharmacology and Experimental Therapeutics at Tufts University, is Dean at Sackler School of Graduate Biomedical Sciences, is Academic Dean at Tufts Medical School and is Director and Chairman of the Board for the Center for the Study of Drug Development. In addition, he currently sits on the editorial board of over 20 medical publications.

FR. WILLIAM T. LEONARD is called "Fr. Bill" by all who flourish under his wonderful ministry as the Catholic Chaplain at Fernald. Fr. Leonard was ordained to the Catholic Priesthood for the Archdiocese of Boston in 1969. He served as Parish Priest and Juvenile Court Chaplain at St. Ann's Parish, Somerville where he also worked with children with retardation from 1969-1977. He founded the Somerville Human Services Department in 1976. From 1977 to 1989, Fr. Leonard was Administrator of St. Philip Parish / Warwick House in Roxbury, where he also served as Chaplain to the Solomon Carter Fuller Mental Health Center. In 1989 he was appointed Chaplain at the Metropolitan State Hospital in Waltham. In 1992 he became Chaplain at the Fernald School.

KAREN J. LIAZOS is a Clinical Social Work Supervisor at the Fernald School. She received her BA at Bard College, NY, her MA at Brandeis University and her Masters in Social Work at the University of Connecticut School of Social Work. Ms. Liazos holds 18 years of experience in the fields of mental retardation and mental health.

PETER H. O'MEARA (Project Manager) completed undergraduate work at Villanova University and graduated from Boston College School of Social Work. He has been involved in managing mental retardation services for the Pennsylvania Department of Public Welfare for 18 years and has worked the last 9 years for the Department of Mental Retardation, Commonwealth of Massachusetts, as the Facility Director of the Fernald School. Additionally, Mr. O'Meara services as the Administrator of the Marquardt Nursing Center and oversees a number of statewide contracts that support consumer services. He also serves as the Project Manager for the Task Force.

PAULA J. POTVIN received her B.A. from the University of Lowell and her Masters in Social Work from the University of Connecticut. With over 15 years of experience in the field of mental retardation in various capacities, including 10 years with DMR, Ms. Potvin is currently a social work supervisor at Wrentham State School. Previously, she was employed as a social worker at Hosan Center.

PAUL PROCACCINI is an Instructional Media Specialist and director of the media resource center at the Fernald School in Waltham, Massachusetts. The center provides graphic design, media and audio visual production services for use in public relations, communications and training. Paul is also a freelance graphic designer providing design and print production services to companies in the greater Boston area, Boston University, and Johnson & Johnson in Michigan.

PHILIP R. REILLY received his law degree from Columbia University and his medical degree from Yale University. He is the Executive Director of the Shriver Center for Mental Retardation, Inc. Dr. Reilly is also a clinical assistant in the Department of Neurology at Massachusetts General Hospital, instructor in neurology at Harvard University School of Medicine and Adjunct Professor of Legal Studies at Brandeis University.

JOAN E. RICKETTS has worked at the Fernald School for over 14 years as Assistant to the Director of Social Services and is a member of the Community Development Unit. She also spent 9 years as an Academic Teacher's Aide in the Waltham Public School systems.

GERALD C. RYAN is the Director of Communications for the Department of Mental Retardation. Prior positions include the Director of Publications at Spaulding Rehabilitation Hospital, Director of Public Relations at New England Baptist Hospital and Worcester Hahnemann Hospital.

MARGARET (PAT) SCHWALJE is Administrative Assistant to the Fernald School Facility Director. Previously, Ms. Schwalje was Executive Secretary to a Vice President of Pan American World Airways. She has worked at Fernald for 12 years.

ROBERT SCHIAPANI is the Director of Client Records at Fernald School and has been the primary contact for archival reviews and requests.

BONITA L. STECHER is the Librarian at the Fernald School, Howe Library. She has over 20 years experience as a librarian and over 15 years with DMR. Prior to being Librarian at Fernald, she worked in DMR Region III overseeing libraries at Hogan, Berry and Danvers State Hospital campus.

JOE WRINN is the Associate Director of the Harvard University Office of News and Public Affairs. Previously, Mr. Wrinn worked for United Press International and the *New York Times*. He is a 1977 graduate of Syracuse University.

RADIATION/EPIDEMIOLOGIST EXPERTS

DR. S. JAMES ADELSTEIN graduated from Harvard Medical School in 1953 and earned his Ph.D. from MIT in 1957. He is currently Executive Dean for Academic Programs at Harvard Medical School and Director of the Joint Program in Nuclear Medicine at four

Longwood Area hospitals. He also serves as the Vice President of the National Council on Radiation Protection and Measurement. The Task Force was honored by Dr. Adelstein's serving and providing such an active and committed role in the learning process.

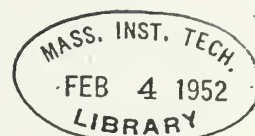
DR. J. DAVID LITSTER obtained his Ph.D. in physics at Massachusetts Institute of Technology. He is currently a Professor of Physics and Vice President and Dean for Research at MIT. He was formerly the head of the Division of Atomic, Condensed Matter and Plasma Physics at MIT. His research field is experimental condensed matter physics. He has provided invaluable assistance to the Task Force on an ongoing basis, including the writing of the Appendix on radiation, calculating the radiation doses in most of the studies, and by working with Doe West on the writing of Section III of this report.

DR. JEFFREY LYON works in the Division of Epidemiology, Biostatistics, and Prevention Research at the Department of Family & Preventive Medicine at the University of Utah. In his prolific writing of articles and research in the fields of radiation biology, Dr. Lyon has studied the long-term effects of radiation exposure in children and adults. He has offered the key research and insight in terms of allowing the medical risk calculations to be done.

DR. BRIAN MACMAHON has been a member of or served as the chairperson of over 50 medical, scientific or health related organizations during his distinguished career as Physician and Professor of Epidemiology. He taught at and served as Head of the Department of Epidemiology at Harvard University from 1958-89 and served as the Editor of "Cancer Causes and Control" for Oxford from 1990-1992. Dr. Macmahon's scientific contributions to the question of risk were again a true cornerstone for the Task Force's understanding.

DR. ROY SHORE received both his Masters Degree and Ph.D. at Syracuse University and his Dr.P.H. from Columbia University. He is a Professor at the Institute of Environmental Medicine at New York University Medical School, NY, NY. In addition, he is the Head of the Environmental Epidemiology Unit. He has written or contributed to over 100 articles to date. Dr. Shore's name was repeatedly suggested to the Task Force as an expert whose opinion was necessary for true insight and clarity.





T.C.

REPORT OF PROGRESS IN RESEARCH

JULY 1, 1944 TO JUNE 30, 1945

NUTRITIONAL BIOCHEMISTRY LABORATORIES
DEPARTMENT OF BIOLOGY
MASSACHUSETTS INSTITUTE OF TECHNOLOGY



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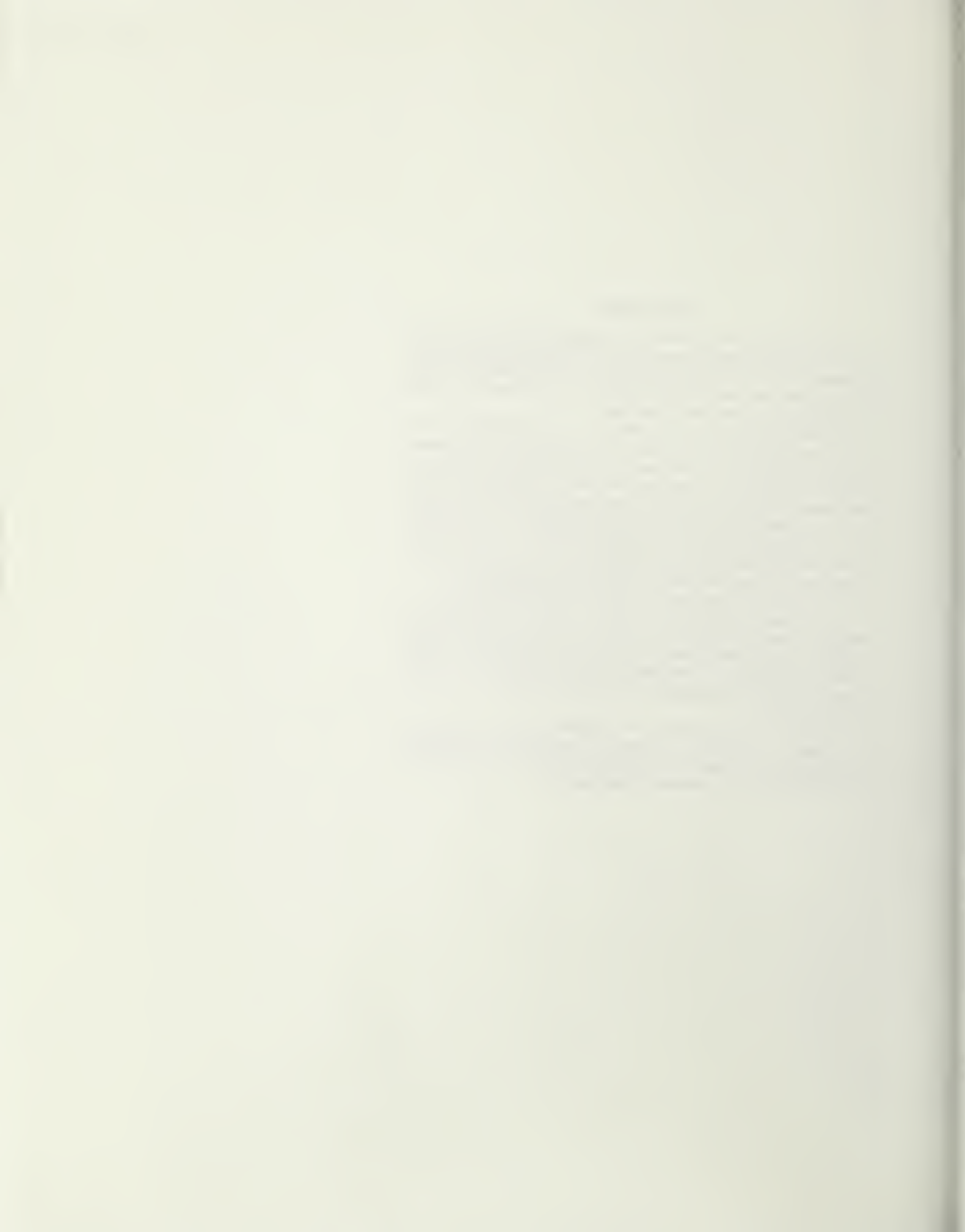
FOREWORD

For the information of friends and supporters of the laboratories this summary of progress in research by the Nutritional Biochemistry Laboratories of the Massachusetts Institute of Technology during the fiscal year just ended has been prepared. We expect to prepare similar summaries each year in the future.

During the past year, the research of the Nutritional Biochemistry Laboratories was generously supported by the Massachusetts Institute of Technology, W. K. Kellogg Foundation, Rockefeller Foundation, Nutrition Foundation, Emma Moore Fund, and Lever Brothers Company. Research during the coming year will be supported by the Massachusetts Institute of Technology, W. K. Kellogg Foundation, Nutrition Foundation, Emma Moore Fund, Lever Brothers Company, Swift and Company, Quaker Oats Company, Hoffmann LaRoche Company, and possibly others.

We wish to take this opportunity to thank foundation sponsors for their generous support and to thank commercial companies for supporting research in the field of their interest without imposing restrictions which would limit our research activities and interfere with the publication of our results. We hope that our research progress has been commensurate with their confidence in our research ability.

Finally, we wish to voice our appreciation for support from Dr. Francis O. Schmitt, In Charge, Department of Biology; to Dr. George R. Harrison, Dean of Science; and to the Administration of the Massachusetts Institute of Technology.



REPORT OF PROGRESS IN RESEARCH

(July 1944 — June 1945)

by the

NUTRITIONAL BIOCHEMISTRY LABORATORIES
DEPARTMENT OF BIOLOGY
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

STAFF OF THE LABORATORIES

The war has not been without its effect upon available research personnel, and we have missed the able services of key personnel. Captain Richard Henderson has been with the Quartermaster Corps of the U. S. Army since 1941, and Pharmacist Mate Albert Nagel has been with the Navy since 1943. We are now hoping for their early return and have continued their names on our masthead.

The staff during the period covered by this summary was:

ROBERT S. HARRIS, S.B., PH.D. (M. I. T.)
Associate Professor, in charge
ERNEST E. LOCKHART, S.B., PH.D. (M. I. T.)
RICHARD HENDERSON, S.B. (M. I. T.), absent
HENRY SHERMAN, B.A. (Harvard)
ELIZABETH W. TAPIA, A.B. (Wellesley)
HELEN S. LOCKHART, B.S. (Boston University)
MARY NUTTER, B.S. (Simmons)
ALBERT H. NAGEL, S.B. (M. I. T.), absent
GERTRUDE NIGHTINGALE, B.S. (Middlebury)
LOUISE GUILD, B.S. (Framingham Teachers)
MARY ANN ARON, A.B. (Illinois), secretary

During the year, Elizabeth W. Tapia and Helen S. Lockhart resigned. Anne F. Knott (B.S., Simmons) and Jane A. Reynolds (B.S., Simmons) were added to the laboratory staff on July 1.

On July 1, Dr. Lockhart was promoted to Assistant Professor.

EXTRA-CURRICULAR ACTIVITIES

In addition to teaching and research activities at the Institute, Professor Harris is serving as Expert Consultant in Nutrition to the Secretary of War and in this connection has supervised the research program of the Nutrition Laboratory at the Pentagon Building in Washington. He still serves on the Committee on the Nutrition of Industrial Workers, of the Food and Nutrition Board of the National Research Council. This committee has prepared a monograph on

industrial nutrition which will soon be published by the National Research Council. He is serving as Expert Consultant to the Foreign Economic Administration in connection with the Relief and Rehabilitation Division, Office of Food Programs, and in this capacity has recently planned a program for the analysis of the major foods in the Chinese dietary. These analyses will be made in our laboratories during 1945-46. In connection with the nutrition programs in Mexico, he is serving as Honorary Consultant to the Mexican Institute of Nutrition and is supervising the research activities of the Laboratory of Bromatology recently established in Mexico City.

Upon request of the Secretary of Health and Assistance of Guatemala, Dr. Harris visited that country in June to make a rapid survey of the nutritional problems of Guatemala, observe present nutrition activities, examine nutrition research facilities and recommend a program for the next few years. He is now preparing a memorandum for the Minister. It is expected that nutritional activities in Guatemala and other Central American countries will be greatly extended during the next year. Our group will likely play a major role in the development of these programs.

Professor Harris has continued to serve as editor of the annual review, "Vitamins and Hormones." Volumes I and II have been published, Volume III will appear in October and Volume IV is in preparation. This book has been very well received by the scientific world.

TEACHING ACTIVITIES

At the present time the Nutritional Biochemistry Laboratories group teaches the following four courses in the department:

- 7.22 Chemistry of Nutrition
2 lectures weekly
- 7.222 Chemistry of Nutrition Laboratory
1 lecture, 4 laboratory hours weekly
- 7.23 Applied Nutrition
2 lectures, 2 laboratory hours weekly
- 7.24 Advanced Nutrition
2 lectures, 4 laboratory hours weekly

The international implications of nutrition are indicated by the extent to which foreign students have studied with us during the past year. During the period of this report, the following have studied with us:

- Arturo Vergara Uribe, M.D., Colombia
State Department Fellow. After one year with us, he returned in September 1944 to become Chief of the Institute of Nutrition of Colombia.
- Jose M. Portilla, M.D., Ecuador
Commonwealth Fund Fellow. He will return early in September to organize, and to become Chief of, the Institute of Nutrition of Ecuador.

Alberto Henriquez, Chile

Coordinator's Office Fellow. He returns in July and is expected to become director of the Laboratory of Bromatology of Chile.

- Aberindo N. Bose, India
- Subodh K. Mukherjee, India
- Syed S. Husain, India
- Amy Ilua Tsiang, China

During the coming year, we will have with us, among others, the following foreign students:

- Luis Alfredo Gomez Arellano, Dr. of Pharmacology, Ecuador, Commonwealth Fund Fellow.
- Phyllis Kuo-chun Fan, China, Kellogg Foundation Fellow.
- Chi-hsuen Shou Tsao, China, Kellogg Foundation Fellow.
- Florence K. C. Wang, China, Kellogg Foundation Fellow.
- Irene Yang-Su Loe, China, Kellogg Fellow.
- Ying Hsueh Wu, China, Kellogg Foundation Fellow.
- Leonel Fierro del Rio, M.D., Mexico.
- Natera Edmundo Rojas, M.D., Mexico, Kellogg Foundation Fellow.

RESEARCH PROGRESS

In the period covered by this summary, research was conducted on: A. The Metabolism of Deuterium-labeled Fatty Acids; B. The Metabolism of Hydroxy Fatty Acids; C. The Composition of Mexican Foods; D. Radium Metabolism and Experimental Osteogenic Sarcoma; E. Nutritional Quality of American Diets; and F. Effect of Large Scale Cooking on the Vitamin Content of Foods.

A. The Metabolism of Deuterium-labeled Fatty Acids

This program has been under way for several years. Its purpose is to study with rats the digestion and metabolism of typical fatty acids; to locate the tissues where these acids are stored, degraded to simpler acids or synthesized into more complex acids; to observe the saturation or desaturation of these acids; to determine the rate of excretion of fatty acid end-products; in effect, to follow the biochemical processes by which food fatty acids are utilized. To do this we "tag" the fatty acids under study with deuterium or heavy hydrogen, synthesize them into triglyceride or fat, and trace their metabolic progress. Involved apparatus has been constructed so that minute quantities of deuterium may be identified in samples of body tissues and in excreta.

During the past year, we have demonstrated that the deuterium technique can be very useful in the study of the mechanism of hydrogenation of fats, and that catalytic hydrogenation is not really selective, although the more unsaturated acids become saturated more rapidly. Animal tests have also shown that it takes about two days for an end-product of fat metabolism to appear in measurable amounts in the urine, and seven days pass before the deuterium content of the

body water of rats fed constant amounts of deuteriumated cottonseed oil reaches equilibrium. Iso-oleic acid, the form of oleic acid commonly found in hydrogenated fats, was proven by the deuterium technique to be readily metabolized. The preliminary observation that dermal tissues contained a disproportionately large amount of "tagged" fat, may be evidence that the skin is more actively involved in the metabolism of food fats than was previously assumed.

B. The Metabolism of Hydroxy Fatty Acids

We have demonstrated with rats that when the fat in a diet already complete in all known nutrients is replaced in part by a triglyceride containing di-hydroxystearic acid, their growth and development is improved (*Archives of Biochemistry*, 5, 63, 1944). Furthermore, there is a tendency for these rats to deposit less fat in the dermal tissues. It would appear that hydroxy fatty acids exert a beneficial effect upon rats, but we have not yet found an explanation for this interesting observation. Hydroxy fatty acids occur in food fats, especially those of animal origin.

We have also reported that the feeding of larger quantities of these hydroxy acid triglycerides provokes a deficiency syndrome in rats which can be prevented or cured by feeding vitamin K (*Science*, 96 (2502), 542, 1942).

Research of the past year on this subject has shown that the kinds and numbers of bacteria in the intestinal tract are the same when the diet contains hydroxy acids as when it does not. The very low content of vitamin K in the caecum and large intestine indicates that synthesis of this vitamin by bacteria is arrested. Thus, it seems that this syndrome results from a disturbance in the metabolism of the bacteria in the caecum and large intestine. The rat is dependent on the vitamin K synthesized by intestinal bacteria, for when this synthesis is disturbed, vitamin K deficiency results.

C. Composition of Mexican Foods

For the past several years these laboratories have been collaborating with the Mexican Institute of Nutrition and the Pan American Sanitary Bureau in the training of personnel, in the analysis of typical Mexican foods, in the establishment of a nutritional biochemistry laboratory in Mexico City and in the formulation of a sound school lunch program in Mexico.

During the first year of this program, three clinicians were trained in the clinical and research aspects of nutrition and two chemists were trained in food analysis. A total of 112 samples of Mexican food were collected, frozen with carbon dioxide ice, and shipped by air express. Working with our staff, the Mexican chemists analyzed these samples for moisture, nitrogen, ash, calcium, phosphorus, iron, thiamine, riboflavin, niacin, ascorbic acid and vitamin A content. The results of this investigation were recently published (*J. Nutrition*, 29 (5), 317, 1945). Also the results of a study of the nutritional values of the Mexican tortilla has been published (*Science*, 102, 91, 1945).

Some exceptional foods were revealed by these analyses. A serving of "malva" (an indigenous spinach-like plant) was found to contain 40 per cent of the N. R. C. calcium allowance, 90 per cent of the iron, 140 per cent of the vitamin A, 60 per cent of the ascorbic acid and significant proportions of the allowances of the other nutrients. "Charales," (an air-dried, small, fresh-water fish) supplied in a 30-gram portion 27 per cent of the protein and 155 per cent of the calcium allowances. "Pulque" (the fermented juice of the maguey cactus) contributed very significant amounts of thiamine, riboflavin, niacin, ascorbic acid and iron. As a whole, the Mexican foods seemed definitely more nutritious than those of the United States. It is clear that with a food pattern so different, any sound Mexican nutrition program should be based on the composition of Mexican foods only. It is interesting to note that our prediction, based on food analysis, that the Mexican diet is weakest in riboflavin and niacin content was confirmed by a clinical study (unpublished) of the people in the Mesquital area by a group from the Rockefeller Foundation.

It was observed that the calcium content of the Mexican tortilla is so high that the average Mexican obtains more than 500 mgs. of calcium in the 280 grams of tortilla he eats each day. It is significant that these people would be calcium-deficient were it not for their native practice of using lime in the preparation of corn for tortillas.

On the basis of these analyses of Mexican foods, a school lunch program was carried out during an entire school year on approximately 1,000 children. Some seven dictaries were used in rotation, each calculated to supply one-third of the N. R. C. allowance to each child. The lunch cost two to three cents daily. This was less than one-fifth as expensive as comparable lunches formulated on the United States food pattern.

The children receiving these lunches lived in the poorest section of Mexico City. The average family size was seven, the family income about 30 cents daily. These children showed no more evidence of malnourishment than a group of 760 middle-class school children studied with the same techniques by our group in Michigan in 1943 (*J. Amer. Diet. Assoc.*, 19, 182, 1943). Poverty does not necessarily breed malnutrition, nor do riches insure against it. The results in Mexico may be explained as due to a racial difference. But we are convinced that the superior quality and the unrefined nature of Mexican foods, and the firmly established food habits of these people are important factors also.

On the basis of our experience in Mexico, an article has recently been published (*Science*, 102, 42, 1945) emphasizing the importance of food analysis to the development of a sound agricultural and nutritional program. We can best help other nations by training personnel, providing equipment, and sending experts to help initiate and maintain research programs. We should not impose our foods or food habits upon them; rather we should make available our knowledge and our skills.

We have assisted in establishing a food laboratory in Mexico and a trained staff is continuing the food analysis program under our supervision. Plans have been made and funds may soon be granted for a similar program in one or several Latin American countries. Chemists, physicians, agronomists and nutritionists will be trained, foods will be analyzed, a bromatology laboratory will be provided and a field study will be conducted. After the above nutrition team is trained and started upon a sound program of research and education, it should be successful in establishing nutrition activities in its country.

D. Radium Metabolism and Experimental Osteogenic Sarcoma

In an effort to determine more accurately the toxicity of radium, we have conducted experiments in which rats have been fed or injected with radium and the effects observed over succeeding months. This work has been summarized in two recent publications (*Am. J. Pathology*, 20, 1-21, 1944; *Am. J. Roentgenology and Radium Therapy*, 52, 353, 1944). Chronic radium poisoning was produced in four series of rats. When 25 to 100 micrograms of radium were given by mouth, primary osteogenic sarcoma resulted in approximately one year. This sarcoma usually developed in the vertebrae and metastases were found in the lung and other organs. These sarcomas have been transplanted to other rats and passed through more than 12 generations. It is our understanding that this is the first successful development of transplantable experimental bone sarcoma. This should greatly assist in bone cancer research.

Four to eight per cent of the radium fed by mouth was still retained after four days. At the end of one year, one to seven per cent remained in the animals' bodies. On the other hand, approximately 50 per cent of the radium injected intradermally was retained at the end of a year. A terminal retention of only one microgram of radium was sufficient to produce osteogenic sarcoma. Over 90 per cent of the retained radium was found in the skeleton, the bone showed 100 times the radium concentration of the richest soft tissue (lung).

It was hoped that the rat would be useful for estimating the toxic dose of radium in man. We have shown, however, that the toxic dose is far greater in the rat than in man. The rat requires 150 times as much radium per kg. body weight and 250 times per kg. skeletal weight. This investigation was made in collaboration with the Department of Physics of M. I. T. and with Dr. Joseph Aub of Harvard Medical School.

E. Nutritional Quality of American Diets

In the past the adequacy of the dietaries of population groups has been measured by one or another type of dietary survey. Though each of these methods has its usefulness, none can accurately predict the actual intake of nutrients by a population. Variation in the nutrient content of each food, in losses during preparation and service, and in the size of servings, combine to make calculation

unreliable. It seemed to us that a laboratory measurement of the dietary intake of nutrients was necessary.

We analyzed the nutrient content of the diets of a selected group of 71 subjects during the latter part of 1943. Concurrently, the 3,336 returns from a dietary survey, that was conducted on a nation-wide basis, were used to estimate the reliability of the data from the smaller group whose diets were analyzed (*J. Am. Diet. Assoc.*, 20, 742, 1944).

The adequacy of the diets was measured by comparison with the Recommended Dietary Allowances of each subject as suggested by the Food and Nutrition Board of the National Research Council (N. R. C. Reprint and Circular Series No. 122, 1945). When so measured, the average daily intake for the group was adequate in ascorbic acid, calcium, and iron, but inadequate in thiamine, riboflavin, and niacin. However, only six per cent of the subjects received the full allowance of all nutrients measured. The percentage of subjects receiving the allowance of each nutrient was as follows: niacin 25 per cent, riboflavin 27 per cent, thiamine 38 per cent, ascorbic acid 52 per cent, calcium 63 per cent and iron 72 per cent.

Only 21 per cent of the subjects received as much as three-fourths of the National Research Council Allowance of all nutrients measured. The following percentage received three-fourths of each allowance: niacin 52 per cent, riboflavin 61 per cent, thiamine 68 per cent, ascorbic acid 71 per cent, calcium 87 per cent and iron 91 per cent.

Less than 35 per cent of the subjects received the more conservative Minimum Daily Requirement as defined by the U. S. Food and Drug Administration.

The dietary survey indicated that the quality of the diets studied by chemical analysis was superior to that of the national sample. Thus, it is probable that the dietary intake of the nation at the time of this study was lower than that reported above, and not as high as several government agencies contended.

Adequacy of nutrition as measured against the National Research Council allowance reveals that few people in the United States were well fed in 1943. There is no reason to believe that it was significantly better in 1944 or 1945.

F. Effect of Large Scale Cooking on the Vitamin Content of Foods

There is considerable interest in the losses of certain vitamins which take place during the cooking of foods. An article from these laboratories several years ago (*J. Am. Diet. Assoc.*, 12, 23, 1943) reported that an average of 45 per cent of the ascorbic acid and 35 per cent of the thiamine of vegetables was lost during large scale preparation and service. In some instances the losses were as high as 96 per cent. Largely as a result of this publication, Dr. Harris was appointed as Expert Nutrition Consultant to the Secretary of War to set up the Nutrition Laboratory in the Pentagon Building in Washington so that a complete investigation of the losses of nutrients in foods during preparation might be made with the

support of the Office of Scientific Research and Development. This laboratory has been in operation for more than one year, and a staff of eight investigators has to date completed studies on potatoes, carrots, cabbage and spinach.

The first report of the results of this laboratory is concerned with the effect of cooking upon the vitamin content of potatoes and will be published shortly.

In the preparation of mashed potatoes, the only important vitamin loss was in ascorbic acid. During mashing, 18 per cent was lost, and during a subsequent 45 minutes on the steam table, 94 per cent was lost. Potatoes showed losses of 11 per cent ascorbic acid during steaming and 19 per cent during standing for one hour. During boiling, 13 per cent of the ascorbic acid content of potatoes was lost, while 21 per cent more was lost while standing on a steam table. During baking, 12 per cent of the ascorbic acid was lost, while 28 per cent more was lost on standing 90 minutes. There were no losses in thiamine and niacin during the steaming of peeled potatoes, and losses of 17 per cent thiamine and 17 per cent niacin during boiling. From the nutritional standpoint, the steaming of potatoes represents the best method of preparation.

It is expected that a series of six or more articles will be published under this laboratory program.

RESEARCH PROGRAM FOR 1945-46

During the coming year, the following subjects will be investigated by our laboratories: A. The Metabolism of Deuterium-labeled Fatty Acids; B. The Metabolism of Hydroxy Fatty Acids; C. The Composition of Ecuadorian Foods; D. The Composition of Chinese Foods; E. The Effect of Phytates upon the Absorption and Excretion of Calcium, Phosphorus and Iron; F. The Effect of Dietary Fat upon Requirement of Amino Acids; and G. The Effect of Large Scale Cooking on the Vitamin Content of Foods. Other subjects may be added as the year progresses.

A. The Metabolism of Deuterium-labeled Fatty Acids

The study of the metabolism of "tagged" fatty acids will continue, with major emphasis upon the metabolism of oleic acid.

B. The Metabolism of Hydroxy Fatty Acids

This investigation will consist of two parts. In one, an *in vitro* study will be made of the effect of di-hydroxy stearic acid upon the synthesis of vitamin K by intestinal bacteria (coli-aerogenes types). We wish to determine the manner in which hydroxy stearic acid interferes with this biochemical process. Possibly it blocks an important enzyme system.

In the second part of this program, we will use white rats and investigate the effect of hydroxy fatty acids upon the gastro-intestinal synthesis of vitamins other than vitamin K, notably thiamine,

riboflavin and niacin. There is no reason to suppose that the effect on these vitamins will be similar.

C. The Composition of Ecuadorian Foods

In collaboration with Dr. Gomez, we plan to analyze food samples from Ecuador. It will be interesting to compare the composition of these foods with that of similar foods from Mexico, for we have already noted that differences in strain may result in marked differences in nutritional quality.

D. The Composition of Chinese Foods

A project has been set up in collaboration with the Foreign Economic Administration, the War Department and the Chinese Government whereby data on the composition of Chinese foods will be obtained. Under this program, Dr. Walker of the Foreign Economic Administration will collect and stabilize samples of more than two hundred foods, taken at several seasons of the year and from various parts of China. The Army Air Forces Command will transport these samples to Cambridge where they will be analyzed by four Chinese in collaboration with our laboratory personnel. These Chinese have been awarded fellowships by the W. K. Kellogg Foundation for a twelve-month period. They will be trained in the methods of food analysis and in nutrition science, with the expectation that they will return later to China and enter the employ of the Chinese Institute of Nutrition. In many respects this program will resemble that which we carried out in collaboration with the Mexican Institute of Nutrition.

E. Effect of Phytates upon the Absorption and Excretion of Calcium, Phosphorus and Iron

For many years certain cereal foods have been accused of interfering with the absorption of minerals. The phytates of foods are held to be responsible for this interference. The literature on this subject is confusing. We propose to study first the effect of relatively pure phytates upon the absorption and excretion of iron, calcium and phosphorus. These minerals will be made radioactive by cyclotron bombardment, incorporated into inorganic salts and mixed in the dietary. The metabolism will be traced by radioactivity-measuring techniques. After this series is completed, we will study the effect of phytates in cereals (oats, corn, rye, etc.) upon the absorption and excretion of these mineral salts. Finally, if we find that phytates do interfere with mineral metabolism, we propose to devise techniques which may be used in the treatment of cereals to minimize the interference. It is possible that the effect of phytates upon the metabolism of minerals in the average dietary is insignificant, but this should be proven.

F. Effect of Dietary Fat upon the Requirement of Amino Acids

Others have shown that a diet poorly balanced with respect to essential amino acid content caused a less satisfactory metabolism

of fat (ketosis) than a diet well balanced in amino acid content. We have hypothesized that the content of fat in the diet may have an influence upon the amounts of essential amino acids required for the growth and development of the rat. We propose to determine whether this "sparing action" exists by using a series of diets, each deficient in a different essential amino acid but adequate in all others, and containing different proportions of fat.

G. Effect of Large Scale Cooking on the Vitamin Content of Foods

The program at the Nutrition Laboratory of the Pentagon is continuing under the sponsorship of the War Department, supported by grants from the Office of Scientific Research and Development. During the coming year, the losses in vitamin content of vegetables and meats during preparation and service on a large scale will be measured. It is expected that this program will be completed within the next year.

PUBLICATIONS

Reprints of publications by members of the staff of the Nutritional Biochemistry Laboratories are available to anyone requesting them. The publications of the past year have been:

1. Harris, R. S. and K. Thiunann: *Vitamins and Hormones*, Vol. II. Academic Press, Inc., 1944.
2. Harris, R. S., H. Sherman and E. E. Lockhart: "Effect of glycerides of hydroxy fatty acids upon growth and development," *Archives of Biochem.*, 5, 63, (Sept.) 1944.
3. Evans, R. D., R. S. Harris and J. W. M. Bunker: "Radium metabolism in rats, and the production of osteogenic sarcoma by experimental radium poisoning," *Amer. J. Roent. Rad. Ther.*, 52, 353, (Oct.) 1944.
4. Lockhart, E. E., R. S. Harris, E. W. Tapia, H. S. Lockhart, M. K. Nutter, V. Tiffany and A. H. Nagel: "Study of the nutritional quality of dietaries by chemical analysis," *J. Amer. Diet. Assoc.*, 20, 742, (Dec.) 1944.
5. Cravioto, R., E. E. Lockhart, R. K. Anderson, F. de P. Miranda and R. S. Harris: "Composition of typical Mexican foods," *J. Nutrition*, 29, 317, (May) 1945.
6. Harris, R. S.: "An approach to the nutrition problems of other nations," *Science*, 102, 42, (July) 1945.
7. Cravioto, R., R. K. Anderson, E. E. Lockhart, F. de P. Miranda and R. S. Harris: "Nutritive value of the Mexican tortilla," *Science*, 102, 91, (July) 1945.
8. Harris, Robert S.: "Reexamining our national nutrition program," New York Legislative Document, 73, 1944.

NUTRITIONAL BIOCHEMISTRY LABORATORIES
MASSACHUSETTS INSTITUTE OF TECHNOLOGY
CAMBRIDGE, MASSACHUSETTS

December 19, 1945

ROBERT S. HARRIS, PH.D.
IN CHARGE
ERNEST E. LOCKHART, PH.D.
RICHARD HENDERSON, S.B.
HENRY SHERMAN, B.A.
HELEN S. LOCKHART, B.S.
MARY NUTTER, B.S.
ALBERT H. NAGEL, S.B.
GERTRUDE NIGHTINGALE, B.S.
LOUISE GUILD, B.S.

Dr. Malcolm Farrell
Fernald State School
Box C
Waverly 78, Massachusetts

Dear Dr. Farrell:

Dr. John W. Chamberlain has informed me of his preliminary conversation with you concerning the possibility of conducting a clinical study at your institution. He has requested me to give you further information as to the purposes of this investigation.

About thirty years ago, it was noted that when dogs were fed a diet high in cereal (notably oats) content, they developed a severe rickets. Subsequent research indicated that this effect was produced because cereals contain large amounts of phytates which form insoluble compounds with calcium that are not absorbable from the gastrointestinal tract. Thus, these cereals interfered with calcium utilization.

Phytates are hexa-phosphate compounds of inositol, a substance which has recently been shown to have vitamin activities. Chemical investigations have revealed that more than 50% of the phosphorus in cereals is combined in the form of phytates.

There has been considerable disagreement regarding the significance of phytates in nutrition, and the information on this subject is very confusing. Even though the data were not yet convincing, the British Government, during the recent war, added calcium carbonate to all flours in order to counteract the possible effect of phytates upon the metabolism of calcium in the British dietary. There is reason to believe that this precaution was unnecessary.

From time to time, nutrition experts and others have advised against the use of large amounts of cereal products in the dietary on the grounds that the phytates contained in these cereals interfere with

- 2 -

calcium metabolism. The poor of the world must eat diets high in cereal content. Thus, it is of considerable importance that we establish the significance of the effect of phytates upon mineral metabolism. We wish first to study the effect of phytates on iron metabolism.

In the past it has been difficult to measure the effect of a factor upon mineral metabolism because the techniques for measuring mineral absorption and excretion have been too crude. The recent production of radioactive minerals by cyclotron bombardment offers a new tool for the study of minerals. It appears that radioactive minerals are metabolized in exactly the same manner as ordinary minerals. Thus, it is possible to tag iron atoms, combine the iron into a compound, feed it and follow its metabolism in the body. Very minute quantities of radioactive substance are required, and the radioactive emanation from this substance is also extremely small.

The emanation is of the same physical character as cosmic rays and the quantities which we would give emit less energy than from the cosmic rays continually bombarding people living at the altitude of Denver, Colorado. This applies only to the regions where there are stores of iron in the body. In connection with blood preparations for the armed forces much larger quantities (3 to 5 times) of radioactive substances have been given to more than 100 medical students. Their blood was checked continually over a period of two years. There were no clinical signs attributable to this radioactive material. There is absolutely no ground for caution regarding the quantities of radioactive substances which we would use in our experiments. The fact that Dr. George Whipple has used these compounds in much greater quantities in his clinical investigations at the Rochester Medical School confirms this statement.

We had first planned to investigate the effect of phytates upon the metabolism of iron and calcium using rats. This would have been better because large numbers of animals could be used and extensive analyses could be performed on various tissues. Unfortunately, data obtained on rats would be of little interest in human nutrition for two reasons. The rat can utilize ferrous and ferric iron with apparently the same ease, whereas human subjects utilize ferrous iron two to twenty times better than ferric iron. Thus, rats differ from humans in their metabolism of iron. Secondly, there is present

- 3 -

in the intestine of rats an enzyme called phytase which has the ability to break down the phytate molecule, whereas the intestinal tract of human beings contains little or none of this enzyme. Thus, rats differ from humans in the manner in which they metabolize phytate.

Because we are interested especially in establishing the significance of phatates in human nutrition, it will be necessary for us to use human subjects. Since it has been shown that iron is absorbed by normal subjects most rapidly during the period of active growth, it is advisable that children be used as experimental subjects. Since human beings vary greatly in their metabolism of these substances, it is necessary that the same subjects be used for the entire series of experiments. Since the previous dietary has an influence upon the absorption and metabolism of minerals, it is important that the previous diet of all subjects used in an investigation be the same. Thus, the experiment requires that we use children who have been in the same institution for at least one month. In selecting the children, it is important that they have no disturbance or abnormality which would interfere with the metabolism of foods.

During the month of January, we propose to run an animal experiment using radio-iron so that we may work out our techniques and establish the procedure for the clinical investigation. It is not possible today to give you a detailed outline of the clinical procedure which we would follow. It is likely that we will want to give the subjects a vitamin supplement during the month of January to make certain that they have no malnutrition, for this might interfere with the absorption and metabolism of iron. On or about February 1, we expect to be ready to initiate the clinical experiment.

This experiment will be divided into five periods. On the first day of the experiment, we would give to each subject several micrograms of radio-iron in the form of ferrous sulfate in an aqueous solution. This feeding would be given early in the morning to subjects who have fasted overnight. Periodically during that day, we would take samples of blood (no more than 5 ml). During the next two or three days, similar samples would be withdrawn. The radio-iron content of the plasma and red cells of each sample would be determined. In this way we can obtain a record of the rate and amount of iron absorption.

- 4 -

After several days have elapsed so that the subjects will be stabilized again, the second period would be started on the same subjects. The second experiment is identical to the first except that a measured quantity of sodium phytate will be fed in the solution containing iron. Blood samples will be withdrawn and analyzed as before. This run will demonstrate the effect of sodium phytate upon the absorption of iron.

In the third period, the same amount of radio-iron will be administered and the same quantity of phytate will be given. However, the phytate will be fed in the form of rolled oats, corn or whole wheat bread. Blood samples will be withdrawn and analyzed as in the other two periods. This experiment will demonstrate the effect of phytates in food upon the absorption of iron.

In the fourth experiment, the same quantity of radio-iron will be fed and this time a diet consisting of the "average American diet" will be fed. Blood samples will be withdrawn and analyzed as before. This experiment will demonstrate whether the amount of phytate in the average diet has a significant effect upon the utilization of iron.

The fifth experiment will be a repetition of the first in order to establish whether the experimental subjects have changed during the period of the investigation.

We believe that these five experiments will take about eight weeks to complete if there are no unforeseen difficulties. In order that we may be certain that ten subjects complete the experiments, we should perhaps start with 15.

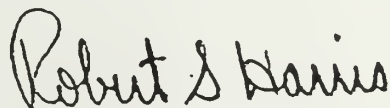
We are planning this investigation so that it will not interfere with the routine of your institution. If there is any way in which we can reward our subjects, we would be glad to do so. If the experiment can be carried out in your institution, we will be glad for any assistance which your medical staff can give us. Of course, we would recognize this assistance when the results are finally published.

We hope that this experiment can be carried out in your institution because the children there would be

- 5 -

ideal for this investigation and because you are convenient to the Massachusetts Institute of Technology laboratories where the analysis of blood samples will be carried out. Professor Robley Evans of our Physics Department is collaborating with us, and the radio-iron will be prepared in the M.I.T. cyclotron. I assure you that the results of this investigation will be of great importance and will influence our thinking in terms of the nutrition of mankind.

Sincerely yours,

A handwritten signature in dark ink, reading "Robert S. Harris". The signature is written in a cursive, slightly slanted style.

Associate Professor of
Nutritional Biochemistry

RSH:maa

DRAFT COPY

March , 1949

Dr. Paul C. Abersold
Isotopes Branch
U.S. Atomic Energy Commission
P.O. Box E
Oak Ridge, Tennessee

Dear Paul:

This letter is to accompany, and to recommend to you for approval, the application by Dr. , Medical Director of the Walter Fernald School, and Professor Robert S. Harris of M.I.T. for Ca-45 to be used in some important fundamental experiments in nutritional biochemistry on selected young, human subjects. All facilities for carrying out the proposed experiment are at hand. The experiments parallel a similar previous study by Prof. Harris and Dr. Sharpe using radioactive iron of cyclotron origin.

The present calcium experiments were originally planned well over a year ago. Since then an exhaustive study of the many factors involved in this calcium experiment has been made using rats, guinea pigs, and dogs, as the experimental subjects. The overall result of this work has been the perfection of experimental techniques in dealing with Ca-45, the experience gained by the research team which is to handle the human nutritional problem, the verification of a number of physical factors relating to calcium uptake and retention, and some detailed knowledge of the degree of nonuniformity of deposition of radiocalcium in various parts of the skeleton. In this connection, for example, Mr. Robert Dudley of my laboratory and Dr. Brown Dobyns of the Massachusetts General Hospital have recently submitted for publication in Science a paper relating to the techniques which they have developed and some of the results obtained in studies of the nonuniformity of deposition of radio-calcium in the skeleton of dogs. By means of calibrated autoradiographs microphotometered in order to determine local variations of radiation dosage, Dudley and Dobyns have shown that local concentrations of radioactivity can give rise to "hot spots" of dosage, and that the dosage rate in such hot spots is about six to ten times the value which would be obtained if all the radioactivity were uniformly distributed in the bone.

I have been personally responsible for at least a year's delay in carrying this experiment on to the case of human nutrition. My feeling was that detailed animal experience should be obtained first. I am now satisfied that this has been done adequately, and that the proposed human experiment can be carried out without going above trivial dosage levels.

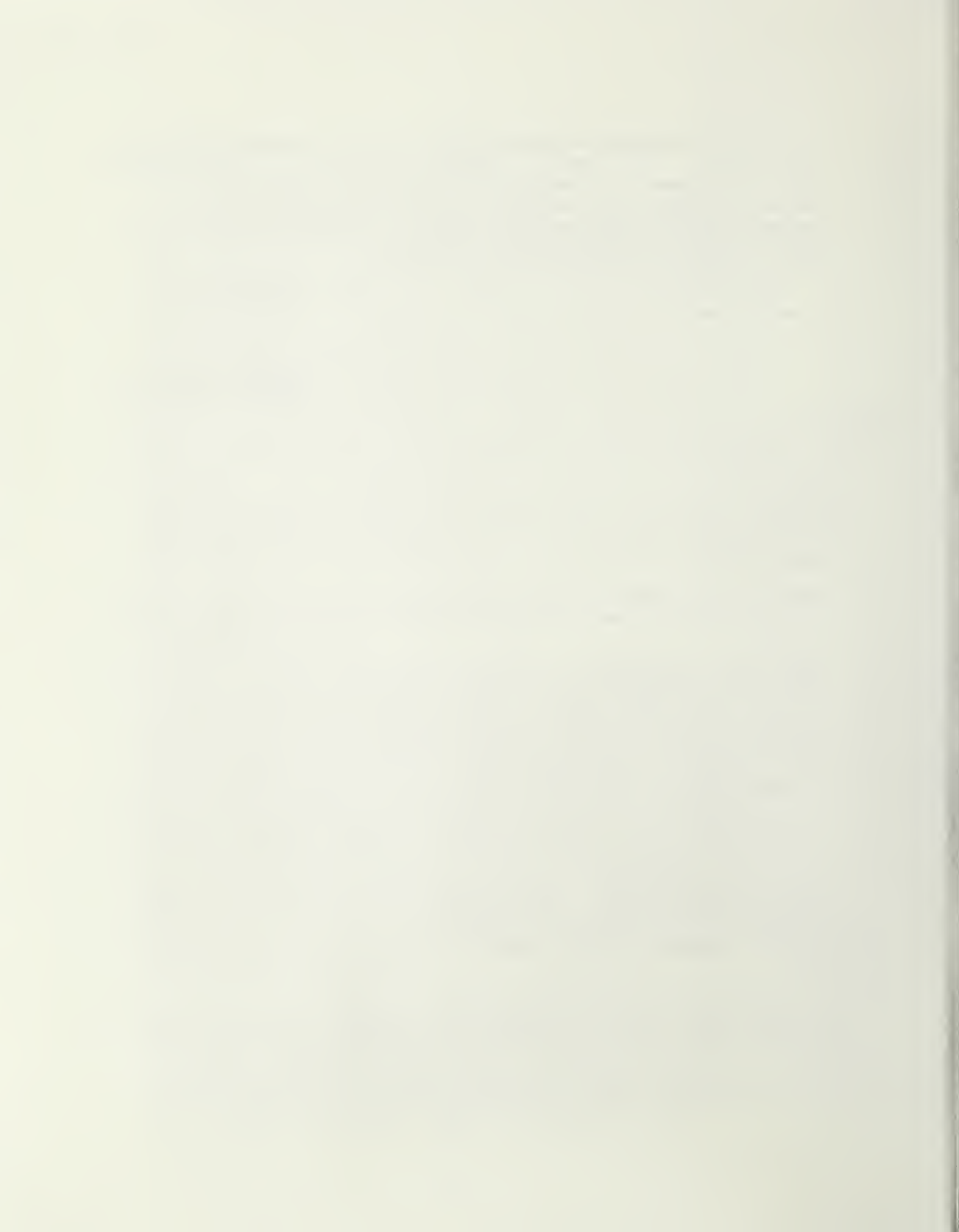
Four simple approaches to the conclusion that the dosages would be adequately small are as follows.

1. It is planned that each human subject will receive 1 μc of Ca-45, mixed with the 250 mg of calcium which is the content of the normal single meal under experimental study. All patients would be on calcium balance and would be receiving the normal 750 mg of calcium per day. From previously available data on humans, obtained by nonradioactive methods, it appears that about 25 percent of the administered calcium may be retained in the growing human. This factor is, if anything, slightly higher than would be expected from our observation of the calcium retention in a young growing dog to which calcium of high specific activity was administered. Assuming, then, that 0.25 μc of calcium is retained in the skeleton, it follows from the so-called "60-formula" that the average bone dose would be expected to be 0.25 millirep/day. This is just equal to the dosage at sea level from cosmic rays and local gamma radiation. It will be remembered that the dosage rate in the blood stream due to the potassium content of red cells is 0.1 millirep/day. Taking hot spot concentrations as giving as much as ten times this average dose, the highest local dosages expected would be of the order of 2.5 millirep/day.
2. As Ca-45 has a half period of 160 days, the time integral of the dosage would amount to only 0.6 in the hot spot areas, and only 0.06 rep of average dose to the bone.
3. One might ask approximately what quantity of radium should be swallowed in order to give a radiation dose which is roughly comparable to that given by 1 μc of Ca-45. Recalling that the average beta ray energy of Ca-45 is about 0.08 Mev, and that the total alpha ray energy of Ra, Rn, Ra-A, Ra-C totals about 15 Mev, taking a low relative biological effectiveness of about 5, and making the conservative assumption that the fractional uptake of calcium might be as much as ten times the fractional uptake of radium, one would infer that 1 μc of Ca-45 would be the approximate equivalent of $(0.08/15) \times (10) \times (1/5) = 0.01 \mu\text{c}$ of Ra. In the field of radium poisoning, where the smallest amounts of fixed radium which have been observed to have deleterious effects are of the order of 1 μc of radium, and where the fractional uptake is usually of the order of 2 percent, the swallowing of 0.01 μc of radium would probably never be viewed with alarm.
4. Karl Morgan's calculation (J. of Phys. and Colloid. Chem. 31, 984 (1947)) indicated a drinking water tolerance of $3.5 \times 10^{-3} \mu\text{c}/\text{ml}$ water. The average daily water intake being about 1.5 liters, this this would amount to a daily intake of about 5 μc . Because the presently proposed nutritional experiment contemplates a single administration of 1 μc , I should be inclined to regard it as perfectly safe.

Because these rough estimates of the dosage all lead to such extremely small values, I have thought it unnecessary for Dr. _____ and Prof. Harris to encumber their application by appending a full report on the animal experiments which have been carried out during the past year. However, I am sure that the animal data can be supplied promptly in case you or other feel that they should be submitted.

Cordially yours,

Robley D. Evans
Professor of Physics





The Commonwealth of Massachusetts
Department of Mental Health

CLIFTON T. PERKINS, M. D.
 COMMISSIONER

ROOM 701, 100 NASHUA STREET, BOSTON, 14

December 27, 1945.

RECEIVED

DEC 29 1945

Walter E. Fernald State School
 WAVERLY, MASS.

Malcolm J. Farrell, M. D., Supt.
 Walter E. Fernald State School -
 Waverley, Massachusetts

Dear Dr. Farrell:

Acknowledgment is made of receipt of your letter and attachments of December 22nd, concerning a proposed piece of research in connection with the Nutritional Biochemical Laboratories of the Massachusetts Institute of Technology.

Perhaps you have not yet become familiar with our procedure in research activities. These proposed activities go through the Advisory Council on Research and Teaching and it well may be that that Committee would invite you to be present at the time when they consider this proposal. Dr. Yakovlev has sat in at those meetings from time to time and undoubtedly would clarify the situation for you. I believe that the next meeting is on the third Thursday of January.

Pending the official meeting I see no objections to your selecting the fifteen or so patients, obtaining the necessary family approvals, and going through the preliminary stage of giving them the extra vitamins during January prior to the actual research work to start early in February.

I'll send your Protocol to Dr. Tadgell as Secretary of the Advisory Committee and have no doubt but what it will be considered at the next meeting.

Very truly yours,

Clifton T. Perkins
 Clifton T. Perkins, M. D.
 Commissioner

CTP:HFT

*The Commonwealth of Massachusetts**Department of Mental Health***RECEIVED**COMMITTEE ON PSYCHIATRIC EDUCATION
AND RESEARCH

DEC 31 1945

Walter E. Fernald State School
WAVERLEY, MASS. DOGELL, M.D.
SECRETARYHARRY C. SOLOMON, M.D.
CHAIRMAN

December 29, 1945

Malcolm J. Farrell, M. D.,
Walter E. Fernald State School,
Waverley, Massachusetts

Dear Dr. Farrell:

Doctor Perkins has forwarded to me the material concerning the proposed research study to be made in conjunction with the M. I. T. Nutritional Biochemistry Laboratories. This matter will be brought before this Committee at its next regular Meeting which is scheduled for Thursday, January 24, 1946.

As Secretary, I am taking the liberty of inviting you to be present. The informal Meeting will be held at the Hotel Kenmore, Boston, at 5:30 P. M., in the lounge-room. Dinner will take place at 6:30 P. M., and, after dinner, the Committee will repair to the Boston Psychopathic Hospital (Dr. Solomon's office) for the Scientific Session.

I trust you can arrange to be with us. An official notice will be sent to you about the middle of January.

Greetings of the Season.

Very truly yours,

Henry C. Dogell M.D.,

HAT:SJG

Secretary



CLIFTON T. PERKINS, M.D.
COMMISSIONER

The Commonwealth of Massachusetts
Department of Mental Health

ROOM 701, 100 NASHUA STREET, BOSTON, 14

March 29, 1946.

Malcolm J. Farrell, M. D., Supt.
Walter E. Fernald State School
Waverley, Massachusetts

RECEIVED
MAY 1 1946
Walter E. Fernald State School
Waverley, Mass.

Dear Dr. Farrell:

On March 27th, I received a copy of the Minutes of the Meeting of the Advisory Committee on Psychiatric Education and Research, which meeting was held at the Boston Psychopathic Hospital on January 24, 1946. This was the meeting at which you discussed the proposed research work of a collaboration nature between the Walter E. Fernald State School and the Nutritional Biochemistry Laboratories at the Massachusetts Institute of Technology. The proposed research was unanimously approved by the Advisory Committee, and the department concurs in that approval.

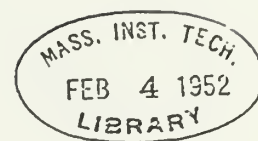
It is my understanding that you have already encouraged some preliminary steps and I see no reason for your not proceeding in the research at the full and proper level.

Sincerely yours,

Clifton T. Perkins
Clifton T. Perkins, M. D.
Commissioner

CTP:HFT





REPORT OF PROGRESS IN RESEARCH

REPORT II

JULY 1, 1945 TO JUNE 30, 1946

NUTRITIONAL BIOCHEMISTRY LABORATORIES
DEPARTMENT OF FOOD TECHNOLOGY
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

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FOREWORD

One year ago the Nutritional Biochemistry Laboratories of the Massachusetts Institute of Technology published its first "Report of Progress in Research" covering the year ending June 30, 1945. This report contained an account of the research and teaching activities of the staff, briefly summarized the year's research activities, and outlined the program for the year ahead. This report was prepared so that those interested in the work of our laboratories might have a periodic summary of research progress. It was so well received that we have prepared this second report, covering the period July 1, 1945 to June 30, 1946.

During the past year the research of the Nutritional Biochemistry Laboratories has been generously supported by the Nutrition Foundation, Inc., the W. K. Kellogg Foundation, the Central American Nutrition Foundation (United Fruit Company), Lever Brothers Company, Quaker Oats Company, Swift and Company as well as the Massachusetts Institute of Technology. Research during the year 1946-47 will be supported by the Nutrition Foundation, the Central American Nutrition Foundation, the Chicago Livestock and Meat Board, Quaker Oats Company, Swift and Company, Hoffman LaRoche, Inc., the Charles H. Hood Dairy Foundation and possibly others.

We grasp this opportunity to thank the foundations and commercial companies who support our research program without imposing restrictions which would limit our activities or the dissemination of our research results by publication in scientific journals. We trust that our progress has justified their investment in our research program.

We have deeply appreciated the support and encouragement which Prof. William L. Campbell, head of the Department of Food Technology and which the administration of the Massachusetts Institute of Technology has given our program.

THE STAFF OF THE
NUTRITIONAL BIOCHEMISTRY LABORATORIES



REPORT OF PROGRESS IN RESEARCH

(July 1, 1945 — June 30, 1946)

by the

NUTRITIONAL BIOCHEMISTRY LABORATORIES
DEPARTMENT OF FOOD TECHNOLOGY
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

STAFF OF THE LABORATORIES

The staff during the period covered by this summary was:

ROBERT S. HARRIS, S.B., Ph.D.
Professor in Charge
ERNEST E. LOCKHART, S.B., Ph.D.
HAZEL E. MUNSELL, B.A., Ph.D.
RICHARD HENDERSON, S.B.
HENRY SHERMAN, B.A., Ph.D.
LOUIS O. WILLIAMS, B.A., Ph.D.
MARY NUTTER, S.B.
GERTRUDE NIGHTINGALE, B.S.
LOUISE GUILD, B.S.
ANNE F. KNOTT, S.B.
SAMUEL A. GOLDBLITH, S.B.
ISABEL MACCLELLAN, Secretary

During this period Mr. Sherman received his Ph.D. degree and Professor Harris was advanced to a full professorship. The Laboratories were transferred from the Department of Biology to the Department of Food Technology on March 1, 1946. Dr. Hazel E. Munsell joined the staff on May 1. Mr. Henderson was honorably discharged from the Army in March with a rank of Major in the Quartermaster Corps after four years with three years' service in Australia. Mr. Goldblith was honorably discharged in February with the rank of Captain. Three and a half years of his four years of service were spent as a prisoner of war in Bataan and in Japan. He received a citation for gallantry in action and was awarded the Silver Star medal.

Messrs. Richard Henderson, Merton P. Lamden and Leon M. Sharpe are conducting research for use in their theses to be submitted for credit toward degrees of Doctor of Philosophy.

EXTRA-CURRICULAR ACTIVITIES

Professor Harris continued to serve until October 1, 1945, as Expert Consultant to the Foreign Economic Administration and as

Expert Consultant in Nutrition to the Secretary of War through June 30, 1946. He is still serving as a member of the Committee on Nutrition of the Pan American Sanitary Bureau and in that connection is taking a leading part in organizing the Institute of Nutrition of Central America and Panama and in planning the first four years of its program.

In connection with this program, a chemist, a physician, an agronomist and a nutritionist from each of the participating countries will be granted a one year fellowship for study in the United States. A large laboratory will be established in Guatemala City for the analysis of native foods as well as sample diets taken in the various countries. This laboratory will be directed by a chemist from the United States. The physicians and nutritionists will collaborate in a field study of the nutritional and clinical status of the population in one area so that they may develop their skills in survey work under the leadership of an American physician.

The INCAP is to be a permanent organization concerned with food and nutrition problems of Central America. It will be directed by an executive board consisting of one member from each country, one from the Pan American Sanitary Bureau and one from the Kellogg Foundation which is providing funds for the fellowship program and for the equipment of the laboratory. This is an interesting opportunity for international collaboration on an important problem, for nutrition and malnutrition are not limited by political boundaries or racial inheritance.

The Charles H. Hood Dairy Foundation has appointed Dr. Harris to its Advisory Committee for a period of five years.

TEACHING ACTIVITIES

The following four courses were taught by members of the staff of the Nutritional Biochemistry Laboratories:

20.04	Chemistry of Food
	2 lectures, 4 laboratory hours weekly
20.32	Chemistry of Nutrition
	2 lectures weekly
20.322	Chemistry of Nutrition Laboratory
	1 lecture, 4 laboratory hours weekly
20.34	Applied Nutrition
	2 lectures, 2 laboratory hours weekly
20.36	Advanced Nutrition
	2 lectures, 4 laboratory hours weekly

The following foreign students have studied with us and worked in our laboratories during this period:

Leonel Fierro del Rio, M.D.
A professor of bromotology at the Institute of Tropical Diseases, Mexico.

Luis Alfredo Gómez Arellano, Doctor of Pharmacy.
Ecuador, Commonwealth Fund Fellow. Dr. Gómez will return home to direct the Laboratory of Bromotology of the Institute of Nutrition of Ecuador.

Subodh K. Mukherjee, India Fellow.
Lenore Yang-Su Loc, China, W. K. Kellogg Foundation Fellow.

Chi-hsuen Shou Tsao, China, W. K. Kellogg Foundation Fellow.

Florence K. C. Wang, China, W. K. Kellogg Foundation Fellow.

Ying Hsueh Wu, China, W. K. Kellogg Foundation Fellow.

When the training of the above four Chinese students is completed, they are to join the staff of the food laboratory of the National Institute of Health in Peiping, China, and continue the program of analysis of Chinese foods which was initiated by our laboratories.

The following distinguished persons visited our laboratories during the year:

Mr. Dinor Walter Invernizzi, Montevideo, Uruguay.

Dr. Salvador Zubiran, Rector de la Universidad Nacional Autònoma de Mexico, Mexico.

Dr. B. C. F. Jansen, Holland.

Dr. Hsien Wu, Director of the Chinese Institute of Nutrition.

Dr. F. W. Clements, Australian Institute of Anatomy.

Dr. Eleanor D. Mason, Department of Physiology and Nutrition, Women's Christian College, Madras, India.

RESEARCH PROGRESS

During this period research was conducted on: A. The Metabolism of Deuteriumated Oleic Acid; B. Effect of Hydroxystearic Acid upon the Intestinal Synthesis of Vitamins; C. Effect of Fat upon Nitrogen Retention; D. Composition of Chinese Foods; E. Composition of Central American Foods; F. Composition of Ecuadorian Foods; G. Effect of Large Scale Cooking on the Vitamin Content of Foods.

A. Metabolism of Deuteriumated Iso-Oleic Acid

Deuteriumated iso-oleic acid was fed in the diets of rats. There was an increase in the iodine numbers of the fatty acids in the carcasses and hides as well as in their deuterium content, indicating that the food fat was deposited in the body depots. On the basis of the deuterium content, the liver fatty acids were more rapidly replaced than the fatty acids of other tissues confirming previous reports that the liver plays an important rôle in fatty acid metabolism. The appearance of large amounts of fatty acid containing deuterium in the kidneys indicated that the composition of kidney fat may be rapidly affected by dietary fat. The low deuterium content of the brain fatty acids demonstrated that the rate of change of the character of the fat in this organ is relatively slow.

In terms of total fat metabolism the liver may not be the most important metabolic tissue and dermal fat and carcass fat may be much more important in fat metabolism than was once thought. There were 40 grams of fat in the hides and 50 grams of fat in the carcasses to every gram in the liver.

The presence of deuterium in the saturated fatty acids in the carcass demonstrates that the rat can hydrogenate iso-oleic acid. The presence of deuterium in the urine and body fluids proves that the organism can metabolize iso-oleic acid.

Spectrophotometric analyses of the carcass and hide fatty acids demonstrated that arachidonic acid had been synthesized. It has been thought that this "essential" fatty acid cannot be synthesized by the rat and must be supplied in the diet. Our data suggests that the rat can synthesize this acid if certain non-essential fatty acids are supplied in the diet. The octabromide of arachidonic acid contained deuterium, further proof of the synthesis of this fatty acid. The demonstration of "essential" fatty acid synthesis is of considerable importance.

B. Effect of Dihydroxystearic Acid upon Intestinal Synthesis of Vitamins

The manuscript on the "Effect of Dihydroxystearic Acid on Vitamin K Synthesis by Rats" has been completed and will be presented before the meeting of the American Chemical Society in September and published shortly afterward. In this paper it was reported that vitamin K deficiency developed more rapidly in male than in female rats receiving the hydroxy fatty acid; that no vitamin K was present in the intestines of these rats, indicating an arrest in vitamin K synthesis; that neither the kinds nor numbers of intestinal bacteria were affected by the fatty acid feeding, indicating that the deficiency syndrome did not result from a bactericidal or bacteriostatic action upon the intestinal flora but possibly from a blocking of the biochemical system involved in the synthesis of vitamin K; and that the physiological requirement of the male rat for vitamin K is higher than that of the female rat.

The studies of the effect of dihydroxystearic acid upon the intestinal synthesis of thiamine, riboflavin and niacin have not yet been completed. The results to date seem to indicate that the synthesis of these vitamins is unaffected.

C. The Effect of Fat upon Nitrogen Retention

We are studying the effect of the level of fat in the diet upon the metabolism of a protein (gelatin) deficient in several amino acids, when fed in diets otherwise adequate to rats. The results of the nitrogen balance measurements in the first trial indicated that the fat in the diet had caused a sparing action and that this sparing action increased as the fat content was increased toward 20 per cent of the diet. The sparing action decreased again when the diet contained 30 per cent fat.

When the experiment was repeated, using sugar in this diet in place of cornstarch, no sparing action was noted; in fact, the nitrogen balance became more negative as the fat content of the diet was increased. This may indicate that the sparing action of fats is affected by the nature of the carbohydrate component of the diet. At the moment it is difficult to interpret the series of experiments that have been run in this study.

It is interesting that the groups of rats consumed iso-caloric quantities of diet each day in spite of the fact that they were fed *ad libitum* and that they were fed several varieties of diet.

D. Composition of Chinese Foods

In collaboration with the Foreign Economic Administration, the U. S. War Department and the Chinese Institute of Nutrition, samples of food have been collected in China and shipped to the United States by air for analysis in our laboratories. Four Chinese chemists, provided with fellowships by the W. K. Kellogg Foundation, were trained in our laboratories in the methods of food analysis and assigned to analyze the foods. The program had started when hostilities ceased and the program immediately lost its importance to our armed forces. However, the project was allowed to run for the full year because the data would be useful to relief agencies and to the Chinese Government.

Fifty-six foods were analyzed for moisture, ash, nitrogen, calcium, phosphorus, iron, carotene, thiamine, riboflavin, and niacin content. Several of the foods were found to be especially nutritious.

Mu-erh (Anricularie annicula-judae-Schrot) was the most notable, as this fungus contained considerable amounts of protein, iron, calcium and niacin. The iron content (185 mgs. per 100 gms.) is the highest of any food known to us. The blossom of the day lily (*Hemerocallis flava* Z.) is important especially because of its high calcium and iron content. Soybeans, peas, horse beans, kidney beans, apricot kernels and peanuts are also high in nutrient content. Analyses of several soybean products revealed that procedures used in their preparation often increased the nutrient content.

The results of this study of Chinese foods are included in a manuscript now in preparation for publication.

E. Composition of Ecuadorian Foods

A number of samples of staple foods was received from Ecuador and analyzed for nutrient content by Dr. José Portilla and Dr. Alfredo Gómez, working under our direction. Chochoes were rich in nitrogen (6.4 per cent) and calcium (135 mgs. per cent), peanuts were rich in nitrogen (5.2 per cent) and niacin (19 mgs. per cent), lentils were rich in iron (15.3 mgs. per cent) and cocoa was rich in iron (14.8 mgs. per cent). It is expected that this study will be continued in the laboratory to be established in Ecuador.

F. Effect of Phytates upon Absorption of Radioactive Iron

This investigation was designed to demonstrate the extent to which the phytates contained in cereal (oats) interferes with the

absorption of iron from the intestinal tract of children. It is the current belief that phytates (hexa-phosphoric acid salts of inositol) react with minerals in foods to form insoluble mineral salts which are unabsorbable. Radioactive mineral compounds can be used to study this effect. By determining the radioactivity of the haemoglobin taken subsequent to feeding radioactive iron with phytate-containing food, it is possible to determine the rate and extent of the uptake of iron from the intestinal tract. If these data are compared with similar data from experiments in which no phytates are given, it is possible to estimate the extent to which these phytates interfere.

In our experiment we are using a group of 18 children, 10 to 14 years old. In five successive periods equal amounts of iron were fed in (1) a breakfast, (2) a glass of milk, (3) a serving of oatmeal, (4) a glass of milk to which sodium phytate was added, and (5) a glass of water. The feedings in periods (1), (3) and (4) contained equal amounts of phytates and the remaining two contained none.

This investigation is still continuing. Preliminary results indicate that phytates impair the effectiveness of iron absorption and that this interference is much greater when phytates are administered in solutions than when they are fed with food. It was noted that foods, per se, markedly interfere with iron absorption. For example, only two-thirds as much iron was absorbed when administered with milk as with water.

G. *Effect of Large-Scale Cooking on the Vitamin Content of Food*

This study was conducted in the Nutrition Laboratory of the War Department in the Pentagon, Washington, D. C., under the supervision of Dr. Harris in his capacity as Expert Consultant to the Secretary of War. Dr. Munsell was a prominent member of the staff of the Nutrition Laboratory and directed its research for part of the year, before coming to Cambridge.

A marked destruction of ascorbic acid was noted when carrots were steamed and still greater losses were noted when carrots were boiled. Further destruction of this vitamin was noted when cooked carrots stood on the steam table for one hour.

Steamed carrots lost about 18 per cent, and boiled carrots lost 20 per cent to 50 per cent of their thiamine, riboflavin, niacin, pantothenic acid and biotin content. Most of the vitamins "lost" were found in the cooking water. Only slight losses of the B-vitamins and carotene were noted when carrots were held for one hour on a steam table. Carotene losses were less than seven per cent on boiling or steaming.

From the standpoint of flavor, aroma, consistency and appearance as well as retention of vitamins, steaming of carrots is recommended as superior to boiling. Furthermore, carrots should be cooked without peeling.

Similar studies on spinach, cabbage, corn and various cuts of meat have also been studied and manuscripts are being prepared for publication.

During the coming year research on the following subjects will be conducted by our laboratories: A. The Metabolism of Deuterium-labeled Oleic Acid; B. The Synthesis of Essential Fatty Acids by the Rat; C. Effect of Dihydroxystearic Acid upon Intestinal Synthesis of Vitamins; D. Effect of Fat upon Nitrogen Retention; E. Composition of Central American Foods; F. Effect of Phytates in Oats on Absorption of Radioactive Iron; G. Effect of Timing upon the Metabolism of Essential Amino Acids; H. Browning of Ascorbic Acid when Treated by Heat; I. Vitamin Losses in Foods Cooked by Procedures Common in China. Other subjects may be added from time to time.

A. *Metabolism of Deuterium-labeled Oleic Acid*

This study will continue with the expectation that the research on deuterium-labeled oleic acid will be completed and research on deuterium-labeled stearic acid initiated.

B. *Synthesis of Essential Fatty Acids*

We propose to investigate further the biological synthesis of arachidonic acid hoping to determine its precursor. First we will compare the role of oleic acid with that of elaidic acid in effecting this synthesis.

C. *Effect of Dihydroxystearic Acid upon Intestinal Synthesis*

The investigation of the effect of this acid upon the intestinal synthesis of thiamine, riboflavin, and niacin will be completed during the coming year. Concurrently we will observe the effects of a deficiency of each one of these B-vitamins upon the intestinal synthesis of the other two.

D. *Effect of Fat upon Nitrogen Retention*

We are studying the effect of the nature of the carbohydrate component of the diet upon the sparing action of fat on nitrogen retention. These results will aid in interpreting the data of the previous experiments and in planning future work on the sparing action of fat on protein.

E. *Composition of Central American Foods*

We have received a generous grant from the United Fruit Company which will enable us to make a three year study of the composition of all foods grown in Central America. One of our staff is now in that region, observing the foods eaten by the people, collecting specimens for botanical identification, stabilizing samples so that they may be shipped to Cambridge by air, and making valuable observations of the food habits of the people. He will cover all parts of Central America and collect samples of all foods in each region. It is hoped that the program will be completed within three years and that reliable data on several samples of each important food will be obtained. The data will be published in scientific journals from time

to time. At the termination of this program we wish to assemble all the published data on the composition of Central American foods so that this information may be available in one reference source.

We feel that results of this food analysis program will have an important effect upon the food and nutrition problems of these countries. A knowledge of the composition of foods should help the farmer to decide the crops he should plant and the genetic strains he should select so that the harvest may be most nutritious as well as most abundant, should help the nutritionist in determining dietaries which will give the best nutrition for the lowest cost, should help agricultural economists in formulating national policies, and should assist all people toward a more efficient use of available plant and animal products.

F. Effect of Phytates in Oats on the Absorption of Radioactive Iron

This investigation should be concluded within the next year. We are hoping for additional support so that we may compare the availability of phytates in various cereals and cereal products and possibly devise a method of treatment which would increase the availability of minerals in cereals by a destruction or inactivation of the phytate component.

G. Effect of Timing upon the Metabolism of Essential Amino Acids

A preliminary experiment with rats has indicated that it is important that the protein of each meal be balanced in its essential amino acid content. Zein was the sole protein in these diets. It was supplemented with the two essential amino acids (lysine and tryptophane) in which it is most deficient. Tryptophane was given in equal quantities in the control and test diets. The control group of rats received the lysine supplement in the diet every day while the test group received lysine in the diet every third day and on that day three times as much was given. Thus over a period of weeks, both groups consumed the same diets and only the time at which the lysine was fed was varied. The group fed the test diet (lysine every third day) gained one-third as much weight and consumed less food and showed a poorer nitrogen balance than the group fed the control diet (lysine every day). Thus the timing of amino acid feeding has an effect upon the efficiency of metabolism of food protein. This result may have great significance for it may indicate that not only the food for the week but the food of each meal should be balanced in amino acid content. Experiments using a variety of amino acids and several proteins have been planned so that this important observation may be well substantiated.

H. Browning of Ascorbic Acid when Treated by Heat

The non-enzymatic darkening of citrus products subjected to heat and the question of the relationship of this darkening to loss in ascorbic acid content has led us to investigate the mechanism of color formation in heated aqueous solutions of ascorbic acid. It has been reported in the literature that iso-ascorbic acid

produces color less readily than ascorbic acid and also is oxidized in preference to it. Thus, iso-ascorbic acid may possibly be useful as an anti-oxidant to protect ascorbic acid in foods.

At present it is impossible to differentiate iso-ascorbic acid from ascorbic acid except by biological assay. Since iso-ascorbic acid is only five per cent as active biologically as ascorbic acid it is important that a convenient method of analysis be developed. We will work on this problem during the coming year.

I. Vitamin Losses in Foods Cooked by Procedures Common in China

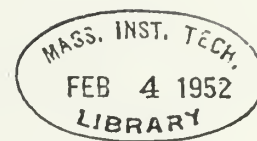
In China foods are commonly cooked by "stir-frying," in which vegetables and meats are cut into thin slices or small cubes and added to a pan containing a shallow layer of hot fat. Since the cooking times of the different components are different, the ingredients are added separately so that the cooking of all will be completed together. Generally, stir-frying requires two to three minutes and the dishes are very flavorful.

This method of cooking may be advantageous from several viewpoints for the cooking time is extremely short and immersion of the food in oil reduces vitamin destruction and the leaching out of vitamins and minerals. We are studying the vitamin losses when foods are cooked according to authentic recipes. Our Chinese fellows will cook the foods and conduct the analyses.

PUBLICATIONS

Reprints of publications by members of the staff of the Nutritional Biochemistry Laboratories are available to anyone requesting them. The publications during the past year have been:

1. Harris, R. S. and K. V. Thimann: *Vitamins and Hormones*, Vol. III. Academic Press, Inc., 1945.
2. Sherman, H., M. K. Nutter, E. E. Lockhart, and R. S. Harris: "Studies on fatty acid metabolism by the deuterium technique. Oleic acid." Abstracts of papers, 109th meeting of American Chemical Society, p. 14A, April 1946.
3. Harris, R. S.: "Nutrient loss through large-scale cooking," *American Cookery*, Vol. 51. No. 8, p. 20, November, 1945.
4. Cravioto, R. B., E. E. Lockhart, F. de Miranda and R. S. Harris: "Contenido nutritivo de ciertos tipos de alimentos mexicanos," *Boletín de la Oficina Sanitaria Panamericana*, Agosto, 1945.
5. Harris, R. S.: "Essentials of a post-war nutrition program," New York Legislative Document No. 70, 1946.
6. Harris, R. S. et al.: "The nutrition of industrial workers," National Research Council, Reprint and Circular Series No. 123 (Sept.) 1945.
7. Munsell, H. E.: "Ascorbic acid content of the mango in relation to variety," *Food Research* 10, 95, 1945.
8. Streightoff, F., H. E. Munsell, B. A. Ben-Dor, M. L. Orr, M. H. Leonard, S. R. Ezekiel and F. G. Koch, "Effect of large-scale methods of preparation on the vitamin content of food: II. Carrots," *J. Amer. Diet. Assoc.* 29 (6), 511, 1946.
9. Goldblith, S. A.: "Sanitation in Bataan and its aftermath," *The Military Engineer*, 1946.



REPORT OF PROGRESS IN RESEARCH

REPORT III

JULY 1, 1946 TO JUNE 30, 1948

NUTRITIONAL BIOCHEMISTRY LABORATORIES
DEPARTMENT OF FOOD TECHNOLOGY
MASSACHUSETTS INSTITUTE OF TECHNOLOGY



1941/1942

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FOREWORD

The previous two "Reports of Progress in Research" of the Nutritional Biochemistry Laboratories of the Massachusetts Institute of Technology have been received so well by our friends that we have been encouraged to prepare this brief summary of the research accomplishments of the past two years, and an outline of the program planned for the year ahead.

During the period beginning July 1, 1946 and ending June 30, 1948, the research program of the Nutritional Biochemistry Laboratories has been generously supported by The Nutrition Foundation, The Central American Nutrition Foundation (United Fruit Company), the Charles H. Hood Dairy Foundation, the National Vitamin Foundation, Hoffman-LaRoche, Inc., The National Live Stock and Meat Board, Swift and Company, Quaker Oats Company, The Procter and Gamble Company, and the Massachusetts Institute of Technology. Our research program during the academic year beginning July 1, 1948 will be supported by The Nutrition Foundation, The National Vitamin Foundation, The Central American Nutrition Foundation, Quaker Oats Company, The Procter and Gamble Company and possibly others.

We welcome this opportunity to express our thanks to the foundations and commercial companies who give financial support to our research program without imposing restrictions which limit either our activities or the publication of the results of our research. We earnestly hope that our progress has justified their investment.

We wish also to voice our appreciation to Professor William L. Campbell, Head of the Department of Food Technology, for his sympathetic cooperation; our thanks to the Administration of the Massachusetts Institute of Technology for its continued support; and to extend greetings to former students, former colleagues and present friends now scattered over the face of the earth.

THE STAFF OF THE
NUTRITIONAL BIOCHEMISTRY LABORATORIES



REPORT OF PROGRESS IN RESEARCH

(July 1, 1946-June 30, 1948)

by the

NUTRITIONAL BIOCHEMISTRY LABORATORIES DEPARTMENT OF FOOD TECHNOLOGY MASSACHUSETTS INSTITUTE OF TECHNOLOGY

STAFF OF THE LABORATORIES

The staff during the period covered by this report included the following:

ROBERT S. HARRIS, S.B., Ph.D.
Professor in Charge
HAZEL E. MUNSELL, B.A., M.A., Ph.D.
HENRY SHERMAN, B.A., Ph.D.
LOUIS O. WILLIAMS, B.A., Ph.D.
*RICHARD HENDERSON, S.B.
*GERTRUDE NIGHTINGALE, B.S.
LOUIS P. GUILD, B.S.
*ANNE F. KNOTT, S.B.
*SAMUEL A. GOLDBLITH, S.B.
*LEON M. SHARPE, S.B.
CYNTHIA B. TROESCHER, S.B.
*MERTON P. LAMDEN, S.B.
*LAURA M. CAMPLING, B.A.
ANDREW C. PEACOCK, S.B.
*RUTH M. EMERY, B.S.
RITA E. BRENZ, B.S.
JUNE WISKIND, B.S.
BOBBE P. FAULDERS, B.S.
ISABEL W. MACCLELLAN, Secretary

Those marked with an asterisk left the staff during the period of this report. Leon M. Sharpe, Richard Henderson and Merton P. Lamden received the Ph.D. degree, and Samuel A. Goldblith the M.S. degree. Dr. Sharpe has joined the staff of Brookhaven Laboratories, Long Island, New York; Dr. Henderson is now Assistant Professor of Bacteriology at Syracuse University; and Dr. Lamden is Assistant Professor of Biochemistry at the University of Vermont Medical School.

PUBLIC SERVICE ACTIVITIES OF THE STAFF

Professor Harris continues to serve as member of the Committee of Nutrition of the Pan-American Sanitary Bureau, and Scientific

Director of the research and training program of the Institute of Nutrition of Central America and Panama. He is chairman of the Cambridge Nutrition Council; a member of the nutrition committee of the Cambridge Red Cross, and of the Massachusetts Central Health Council.

PAPERS PRESENTED AT SCIENTIFIC MEETINGS

During the period covered by this report the following papers were presented at scientific meetings:

- "Effect of Dihydroxystearic Acid on Vitamin K Synthesis by Rats," presented by G. Nightingale. American Chemical Society, September, 1946.
- "The Nutrition Problem of Central America," presented by R. S. Harris, New York State Dietetic Association, May, 1947; also presented before Eastern Massachusetts Dietetic Association, February, 1948.
- "Biological Synthesis of Arachidonic Acid," presented by H. Sherman, American Oil Chemical Society, Chicago, October, 1947.
- "Pyridoxine and Fat Metabolism," presented by H. Sherman. Nutrition Symposium, Columbia University, December, 1947.
- "Program of the Central American Nutrition Foundation," presented by R. S. Harris at Santa Tecla, El Salvador, January, 1948; also presented at Escuela Agrícola Panamericana, Zamorano, Honduras, February, 1948.
- "Estimation of Ascorbic Acid in Food Preparations," presented by S. A. Goldblith, American Chemical Society, New York, September, 1947.
- "Composition of Central American Foods. I. Honduras," presented by H. E. Munsell, American Institute of Nutrition, Atlantic City, March, 1948.
- "Effect of Phytate on the Absorption of Radioactive Iron," presented by R. S. Harris, American Institute of Nutrition, Atlantic City, March, 1948.
- "Use of Isotopes in Biochemical Research," presented by A. C. Peacock, Wellesley College, April, 1948.

TEACHING PROGRAM

The following six courses are taught by members of the Staff of the Nutritional Biochemistry Laboratories:

20.04	Chemistry of Food
20.32	Chemistry of Nutrition
20.322	Chemistry of Nutrition Laboratories
20.34	Applied Nutrition
20.36	Advanced Nutrition
20.38	Nutritional Evaluation of Food Processes

SPECIAL FOREIGN STUDENTS

The following foreign students studied with us and worked in our laboratories during the past two years:

Luis Alfredo Gómez Arellano, D. Pharm., Laboratory of Bromatology, Institute of Nutrition, Ecuador.
 Subodh K. Mukherjee, India.
 Isabel A. Escobar, Hospital de Enfermedades de la Nutrición, Mexico.
 Dr. Sarah Baberly, Hebrew University, Palestine.
 Dr. Walter A. Lindberg, Institute of Hygiene, University of Oslo, Norway.
 Karin M. Wold, Control Laboratory, Pharmaceutical Chemistry, Norway.
 Darshan S. Bhatia, India.
 Nripendra L. Lahiry, India.
 Alfonso C. Parra, Colombia, State Department Fellow.
 Guillermo Arroyave Borjes, Guatemala, Institute of Nutrition of Central America and Panama.
 Salvador A. Pizzati, Honduras, Institute of Nutrition of Central America and Panama.
 Andrés A. Campos, El Salvador, Institute of Nutrition of Central America and Panama.

DISTINGUISHED VISITORS

The following were among the distinguished persons who visited our laboratories during this period:

Prof. Harry Lundin, Institute of Technology, Sweden.
 Dr. A. G. van Veen, Chief of Eijkman Institute, Batavia, Java.
 Dr. M. van Eckelen, Chief of Central Institute for Nutrition Research, Holland.
 Dr. William R. Aykroyd, Food and Agriculture Organization, United Nations.
 Dr. H. E. Magee, Ministry of Health, England.
 Dr. Werner G. Jaffee, Ministry of Agriculture, Venezuela.
 Dr. Maria Szezgel, Warsaw State Institute of Hygiene, Poland.
 Dr. Chium-Tong Ling, National Institute of Health, China.
 Dr. G. Sankaran, Professor of Physiology, All Indian Institute of Hygiene, Calcutta.
 Dr. Guillermo García López, Instituto Coordinador de Nutrición de Cuba, Havana.
 Dr. A. Szezyngiel, State Institute of Hygiene, Department of Nutrition, Warsaw, Poland.
 Dr. Tulio Ganduglia, Buenos Aires, Argentina.
 Dr. Santiago Nadelman, Buenos Aires, Argentina.
 Dr. Karl Wuhrmann, Swiss Federal Institute of Technology.
 Sir Christopher W. M. Coa, Advisor to British Colonial Secretary.
 Dr. F. N. Woodward, United Kingdom Scientific Mission.
 Dr. G. D. Bhavnani, Sind College, Karachi, India.
 Dr. C. K. Chu, Director, National Institute of Health, China.

Dr. Cheng-fu Wong, Director, Institute of Nutrition, China.
 Dr. M. V. Radhakrishnan Rao, Influenza Institute, Bombay, India.
 Dr. Hunt Khumart, Officer in Charge of Food, Military Government, Germany.

Prof. Josué de Castro, Rio de Janeiro, Brazil.
 Dr. S. S. De, Indian Institute of Science, India.
 Dr. S. Wan, National Defense Medical Center, China.
 Dr. K. Cheung, Dean, Army Medical College, China.
 Dr. Sverre Stone, Norwegian Institute of Public Health, Norway.
 Dr. Courado Paseul, Manila, Philippines.
 Dr. Kaj Dessan, Copenhagen, Denmark.
 Dr. A. Ullou Cintra, Hospital Clinics, Brazil.
 Dr. H. C. Hou, Director, Institute of Nutrition, China.
 Dr. P. R. Peacock, Glasgow, Scotland.
 Dr. Edmundo Rojas, Hospital de Enfermedades de la Nutrición, Mexico City.

RESEARCH PROGRESS

A. Metabolism of Deuterium-labeled Iso-Oleic Acid

The use of deuterium to "tag" fatty acids has made it possible to study their metabolic fate. A group of rats was fed a synthetic diet containing fourteen per cent triolein for fourteen days, the given the same synthetic diet, but containing seven per cent triolein and seven per cent tri-di-deuterio-iso-olein for forty-two days. Representative groups were killed periodically during the experimental period and the fatty acids of the carcasses, hides, livers, kidney and brains were analyzed for deuterium content. The results indicated a rapid introduction of the diet fat into the fatty acids of the carcasses, hides, and kidneys, and a slow introduction into the fatty acids of the brain. This confirms data in Report II. The fatty acids in the carcasses and hides became longer and more unsaturated in the experimental period continued. These studies with deuterium-labeled iso-oleic acids indicate that the rat can metabolize iso-acids and that the dermal tissues are actively involved in fat metabolism.

B. Synthesis of Essential Fatty Acids (Arachidonic Acid) by the Rat

In the studies with tri-di-deuterio-iso-olein mentioned under Section A above, the fatty acids from the carcasses and hides were analyzed spectrophotometrically and it was found that the arachidonic acid content of the carcasses fat increased as the experimental period continued. Thus, it appears that arachidonic acid was synthesized by the rats. This conclusion was greatly strengthened by our finding that deuterium was present in the arachidonic acid molecule for it indicated that the arachidonic acid was synthesized from a deuterium-labeled iso-oleic acid in the diet. This evidence that the rat can synthesize an "essential" fatty acid is of considerable scientific interest.

Dr. Sherman has prepared a review of the chemistry and biochemistry of arachidonic acid which will be submitted for publication.

C. Interrelation between Pyridoxine and Arachidonic Acid

When fed a pyridoxine-deficient diet, rats develop a scaliness of the paws and tails which is hardly distinguishable from the syndrome which develops from a deficiency in "essential" fatty acids. Others have demonstrated that pyridoxine is necessary for the formation of fat from protein. From this we have reasoned that there may be an interrelationship between pyridoxine and "essential" fatty acids.

We have demonstrated that this deficiency condition can be cured by feeding pyridoxine but that it is not affected by feeding linoleic acid. The effects of pyridoxine have been confirmed in a repeat experiment. The evidence indicates that pyridoxine deficiency not only decreases the appetite of rats but also the efficiency of food utilization. It appears that rats store only small amounts of pyridoxine, for their growth rate was retarded within five days after they were placed on a pyridoxine-free ration. The rats fed no pyridoxine consumed nearly twice as much food per gram gain in weight as those fed pyridoxine in fat-free diets or in diets containing olive oil. More fat was deposited in their tissues when pyridoxine and/or fat was present in the diet. The dermatitis which developed after two to four weeks on a fat-free pyridoxine-free diet was partially cured by feeding pyridoxine, and completely cured when both pyridoxine and linoleic acid were added. The percentage of arachidonic acid in the carcass fatty acids was lowest when olive oil and pyridoxine were present in the diet of the rats. The total amount of arachidonic acid was greatest in those rats fed pyridoxine in the diet. It is obvious that pyridoxine and arachidonic acid are interrelated in metabolism.

D. Nutritional Value of Elaidic Acid

In the experiments mentioned under Section B of this report both iso-oleic acids and normal oleic acid were present in the diet. The question arises whether the iso-oleic fatty acids were used in the synthesis of arachidonic acid. In an attempt to answer this question one group of rats was given a fat-free synthetic diet; a second group was given this same diet with 14 per cent olive oil (80-85 per cent normal oleic acid) added; and a third group was given this diet with 14 per cent elaidic acid (an iso-oleic acid) added. After 42 days the animals were destroyed, the fatty acids extracted from the carcasses and livers, and these acids analyzed for arachidonic acid content.

The animals on the fat-free diet developed a very mild scaliness of the feet and tails. Since, in a later experiment, this condition was prevented by feeding additional amounts of the various vitamins in the supplement, it is considered possible that olive oil or elaidin in the diet exerts a vitamin-sparing action.

The carcasses of the rats fed the fat-free diet contained definitely less fat, and the carcass fatty acids were more saturated, than those from the rats fed olive oil or elaidic acid. The total arachidonic acid content of these fat samples was determined by both the poly-

bromide and the spectrometric methods. There were approximately 100 mg., 170 mg. and 220 mg. of arachidonic acid per rat as a result of feeding the elaidin, fat-free and olive oil diets, respectively.

On a gram basis, the arachidonic acid content of the carcass fatty acids from the groups fed (1) a fat-free diet, (2) this diet with elaidin or (3) with olive oil was 1.4 per cent, 1.3 per cent and 0.6 per cent, respectively. Further research may show that these differences in the arachidonic acid content of the carcass fats were due to differences in rate of utilization of this acid in metabolism.

E. Effect of Fat Content of Diet upon Nitrogen Retention

A series of diets containing 15 per cent or 25 per cent of gelatine and 0 per cent, 10 per cent, 20 per cent, 30 per cent or 40 per cent of hydrogenated fats, and various carbohydrates (sucrose, dextrose and cornstarch) were fed to rats. The effect of the amount of fat and the type of carbohydrate upon nitrogen retention, growth and food utilization was determined.

The rats tended to eat isocaloric amounts of diets when fed *ad libitum*, even when these diets varied widely (0 per cent to 40 per cent) in fat content. Nitrogen retention increased as the fat content of the diet decreased, and the carbohydrate content of the diet increased. Thus, carbohydrates exert a protein-sparing action. In this study it was noted that the protein-sparing actions of sugar, cornstarch and dextrose are similar.

Tryptophan (0.2 per cent) added to gelatine diets caused an increase in food and caloric intake, a reduction in weight loss, an increase in fat deposition in the liver and carcass, and an increase in nitrogen retention. Diets containing gelatine (25 per cent) as the source of amino acids caused an abnormally low deposition of fat in the livers and carcasses of rats. This effect was counteracted by the addition of 0.2 per cent tryptophan. Tryptophan seems to be involved in the biochemical process whereby fat is deposited in the tissues of rats.

F. Effect of Dihydroxystearic Acid on Thiamine Synthesis and Storage

In a previous study (Arch. Biochem. 12, 381, 1947) it was shown that the synthesis of vitamin K in the intestinal tracts of rats was stopped when dihydroxystearic acid was fed in the diet.

The effect of this hydroxy fatty acid on thiamine synthesis has been studied, and no adverse effect was noted. In fact, there was inconclusive evidence that the thiamine content of the colon and cecal contents, and of the liver and gastrocnemius muscle, was increased as a result of feeding dihydroxystearic acid.

G. Effect of Dihydroxystearic Acid on Riboflavin Synthesis and Storage

A study similar to that mentioned in Section F showed that dihydroxystearic acid in the diet had no effect upon the intestinal synthesis of riboflavin.

II. Composition of the Edible Plants of Central America

On July 1, 1946 a three-year study was begun to determine the composition of the edible plants of Central America. One mem-

ber of the staff is resident there and is responsible for the collection and identification of specimens from all parts of that area in all seasons, and for the preparation and shipment of samples. Procedures have been developed for the stabilization of samples so that they may be air-expressed to Cambridge and analyzed here by four of our staff. Determinations are made of moisture, ether extract, fiber, nitrogen, ash, calcium, phosphorus, iron, carotene (or vitamin A), thiamine, riboflavin, niacin, and ascorbic acid.

As of June 30, 1948, a total of 507 samples had been analyzed and 6932 analyses had been completed. A number of highly nutritious plant food has been "discovered" under this program. The nutrient content of many varieties had not previously been determined by any laboratory.

I. *Nutritional Advantage of the Concurrent Feeding of Essential Amino Acids*

In the past it has been assumed that the quality of the protein is of no importance in one meal, if it is satisfactory during a week, a month or even longer. According to this reasoning, a deficient intake of certain amino acids in one meal may be compensated by an excess intake of these amino acids in subsequent meals. We have long questioned the soundness of this reasoning and have now put it to a test.

Groups of weanling rats were fed a basal diet containing casein (30), cornstarch (55.4), hydrogenated fat (10), tryptophan (0.17), histidine (0.13), salt-mixture (4) and vitamin mixture (0.36). Control groups received the basal diet + 1 per cent lysine. Test groups received the basal diet, and the basal diet + 2 per cent lysine at alternate feedings. The lysine replaced equal weights of cornstarch in the diet. Groups were fed (1) one hour and fasted seven hours, (2) one hour and fasted five hours, and (3) one hour and fasted three hours throughout successive experiments lasting 27 days. A time-interval feeder was devised for the automatic opening and closing of the feeding jars.

Significant differences were noted in nitrogen retention and in body weight gain, weight gain per gram of diet eaten, weight gain per gram of lysine eaten. These differences were greater as the feeding intervals lengthened. Thus a delay of three hours or longer in the feeding of lysine as a supplement to a lysine-low diet interfered with metabolism. Lysine must be fed concurrently with other amino acids in the diet for most efficient utilization by the rat.

The growth and development of the groups receiving the complete diet at every meal was always superior, even when the feeding interval was only three hours. This may be interpreted to mean that the effects of a poor protein in one meal cannot be counteracted by a complementary protein in the next meal; but that a balanced mixture must be consumed at every meal if the protein is to be utilized most efficiently. These results suggest that breakfast foods compounded of several complementary foodstuffs (cereals, legumes, etc.) while superior from the nutrition standpoint, would also be superior dietetically.

J. *Effect of Phytates upon the Absorption of Radioactive Iron*

In this project 17 adolescent boys were used to study the relative absorption of radioactive iron from five test meals: (a) water, (b) milk, (c) milk and rolled oats, (d) milk and sodium phytate, and (e) milk, rolled oats, tomato juice, bread and onion. The iron content of all meals, and the amounts of milk in the last four meals, were the same. Meals (c), (d) and (e) contained the same quantity of phytate; the others were phytate-free.

It was found that the following percentages of the radioactive iron were absorbed, respectively, from the five different test meals: (a) 12.4, (b) 8.3, (c) 4.8, (d) 0.7 and (e) 2.5. These results indicate that milk interferes with the absorption of iron from the gastrointestinal tract. Since the drop in iron absorption when milk and rolled oats was fed was less than twice the reduction produced by milk alone, it is evident that much of the phytate naturally present in rolled oats is inert. The observation that the absorption of iron from a typical breakfast (c) was only one-fifth that from the aqueous solution (a) suggests that medicinal iron would be much more effectively absorbed if taken between meals with water.

This study was undertaken to determine whether the phytates in a typical cereal (oats) interfere with iron absorption. The evidence indicates that phytates interfere but little, and that other factors (such as probably the mass of the food itself) probably are responsible for the relatively poor utilization of food iron.

K. *Vitamin Losses in Foods Cooked by Chinese Procedures*

When vegetables and meats are "stir-fried" by the Chinese method, a shallow layer of fat is heated in a pan to about 280°C. and the diced ingredients are added in such an order that the cooking of all ingredients is completed at the same time. This method of cooking may be advantageous because the cooking time is short (generally 2-3 minutes), little of the vitamins and minerals is leached out and discarded, and the vitamins are protected against oxidation by the oil.

A series of 19 authentic Chinese recipes was used to study the vitamin losses during "stir-frying." Competent Chinese women chemists prepared the dishes and analyzed the foods before and after cooking. Each recipe was prepared in duplicate. One portion was treated with five per cent oxalic acid to preserve it until analyzed, while the second was "stir-fried." In each case the entire recipe (raw or stir-fried) was slurried and the carotene, thiamine, riboflavin, niacin and ascorbic acid content determined by chemical procedures. Results were compared on an anhydrous basis.

The losses varied considerably in the various recipes. The losses in carotene were very low, and in 13 recipes there was an apparent increase. In general, the losses were less than 10 per cent for niacin, 15 percent for riboflavin, 20 per cent for thiamine and 35 per cent for ascorbic acid. These losses compare very favorably with those reported on foods cooked by Western methods.

L. Stability of Solutions of Pure Ascorbic and Dehydroascorbic Acid

The two most acceptable procedures for the analysis of ascorbic acid in foods are the indophenol titration method of Bessey and the phenylhydrazine method of Roe. Frequently, data obtained by these methods do not agree. We have measured the ascorbic and dehydroascorbic acid content of freshly prepared and aged aqueous solutions of pure ascorbic acid, and have compared the stabilizing effects of oxalic acid and metaphosphoric acid on these solutions. The results of these experiments have been published (Science 107, 226, 1948).

It was found that ascorbic acid is stable in 0.5 per cent oxalic-10 per cent acetic acid solutions for at least 12 days at 4°C. In five percent metaphosphoric acid-10 per cent acetic acid solutions it is stable for at least eight days at 4°C. Oxalic acid seems preferable as a preservative for ascorbic acid not only because it is more effective than metaphosphoric acid but also because it is more stable, less expensive and more convenient to use.

Though both metaphosphoric acid and oxalic acid exert a stabilizing effect on ascorbic acid, neither acid prevents the transformation of dehydroascorbic acid into derivatives which are not convertible to ascorbic acid by hydrogen sulfide treatment.

The Roe method (using 2,4-dinitrophenylhydrazine) probably estimates the ascorbic acid originally present in a foodstuff when it was garden-fresh, while the Bessey method (using 2,6-dichlorophenolindophenol) measures only what is biologically active at the time of analysis. This may resolve the controversy on this subject in the literature.

M. Estimation of Ascorbic Acid in Food Preparations

Continuing the research mentioned in the previous section, we have demonstrated that the Roe method and Bessey method are equally valid for measuring the ascorbic acid content in garden-fresh plant materials. More than 90 per cent of the ascorbic acid in the garden-fresh materials studied was in the reduced form. The results of this study have been published (Anal. Chem. 20, 649, 1948).

Samples slurried with four parts of 0.5 per cent oxalic acid and stored for as long as two weeks at room temperature (70-77°F) may be assayed by the Bessey method to determine the ascorbic acid at the time of assay, and by the Roe method to determine the ascorbic acid at the time of harvesting. Thus, by using stabilized slurries of garden-fresh edible plants their ascorbic acid content at the time of harvest may be measured by the Roe method in a laboratory remote from the harvest area. We are applying this method in our Central American food analysis program. These methods may also be used to establish the freshness of vegetable foods.

N. Retention of Vitamins During Cooking of Enriched Farina

Several laboratories have studied the retention of vitamins during the cooking of enriched farina, with discordant results. This question is of considerable importance, since there is little value in

enriching farina with vitamins if large quantities are to be destroyed during cooking.

Three preparations of enriched farina were used in our study. These were prepared individually so that each batch contained known amounts of the enrichment ingredient. The first contained added thiamine, riboflavin, and niacin, the second added thiamine, riboflavin, niacin and a mineral phosphate mixture, and the third added thiamine, niacin and the mineral mixture. Each batch was cooked in a saucepan on an electric stove according to home procedures with care to have this procedure the same for all batches. Each entire batch was slurred for sampling.

The average retentions for the three batches were as follows: thiamine, 98.9, 97.0, 96.6 per cent; riboflavin, 94.9, 98.4, 94.7 per cent; and niacin, 95.2, 100.0, 94.6 per cent. It is evident that less than five per cent of the thiamine, riboflavin or niacin content is destroyed during the cooking of enriched farina by home procedures. The results of this study have been published (J. Amer. Diet. Assoc. 24, 314, 1948).

O. Protein Quality of Certain Foodstuffs

Feeding experiments on 260 male rats showed that (1) the protein of egg albumen and of corn germ is of excellent biological value, (2) the protein of rolled oats is superior to that of soya flour and of Mexican rice, (3) the protein of white corn is inferior to that of yellow corn, (4) the preparation of the Mexican tortilla impairs the nutritional value of the corn protein, and (5) the protein of peanut flour is inferior to that of soya flour. Rats fed uncooked beans died early in the experiment, indicating that the uncooked beans contain a toxic agent, or that they are indigestible.

These results were published in a Mexican scientific journal (Ciencia 7, 203, 1947).

RESEARCH PROGRAM PROJECTED FOR 1948-49

During the coming year research on the following subjects will be conducted in our laboratories: A. The Metabolism of Deuteriated Lauric Acid; B. Nutritional Importance of the Pteridines and Pteroselaidic Acids; C. Metabolic Interrelationships Between the B-Complex Vitamins and Arachidonic Acid; D. Composition of the Edible Plants of Central America; E. Effect of Phytates upon the Absorption of Radioactive Calcium; F. Influence of Liver Extract upon Rats on "Complete" Synthetic Diets; G. Effect of the Iso-oleic Acid Content of the Diet upon Growth; H. Nutritive Values of "Hard" Fats; I. Dermal Absorption of Deuteriated Soaps and Fatty Acids; and J. Synthesis of Glycogen.

A. Metabolism of Deuteriated Lauric Acid

Having completed a study of deuteriated oleic acid we now wish to study other fatty acids which are commonly found in our food fats. Coconut oil is rich in lauric acid. A deuteriated form of lauric acid will be prepared, and its metabolism will be

used using the same procedures as were employed in the deuterium oleic acid study.

B. The Nutritional Importance of the Petroselinic and Petroselinic Acids

Our results with elaidic acid, and the controversial results of others who have worked with vaccenic acid, indicate that the various iso-oleic acids may differ in their nutritional values. We plan to study the nutritional values of oleic acids. Next we will study tripetroselinin and tripetroselaidin, the triglycerides of the cis- and trans-isomers, respectively, of $\Delta^6,7$ oleic acid.

C. Metabolic Interrelationship between the B-Complex Vitamins and Arachidonic Acid

We have already accumulated considerable evidence that pyridoxine and arachidonic acid are interrelated in metabolism and possibly are synergistic. In searching for an explanation of this relationship we plan to test vitamins other than pyridoxine. Each of the B-complex vitamins will be omitted from the diets of rats to determine the effect of each omission upon the arachidonic acid content of tissue fats.

D. Composition of Central American Foods

This fascinating and fundamental survey of the nutritional resources of Central America will continue for another year. Then we plan to write a monograph which will be a discussion of the food plants of Central America from the viewpoint of the botanist, the food chemist and the nutritionist. There remains the problem of stimulating an agricultural and food program in these countries which will lead to a better use of indigenous plant resources.

E. Effect of Phylates upon the Absorption of Radioactive Calcium

Most of the scientific literature on the effect of phytates in foods upon the utilization of minerals is concerned with studies of calcium absorption rather than that of iron, but in no case has the radioactive tracer technique been used to study calcium in relation to this problem. Now that radioactive calcium has been made available from the atomic pile, it is possible to conduct these experiments, but before proceeding with such a study, it must be proven that radioactive calcium is not toxic for human beings. As a preliminary to this program, the absorption and excretion of radioactive calcium will be studied in rats.

F. Influence of Liver Extract upon Rats on "Complete" Synthetic Diets

In a preliminary experiment it has been observed that when a nutritionally "complete" experimental diet, containing liberal quantities of 14 vitamins, was supplemented with liver extract, the male animals were stimulated to grow more rapidly. The female rats seemed unaffected by the liver supplement. The factor in liver which is responsible for the growth of male rats must be investigated.

G. Effect of the Iso-oleic Acid Content of the Diet upon Growth

When oils are hydrogenated in the production of commercial hydrogenated fats, considerable quantities of iso-oleic acids are formed which are different from normal oleic acid in chemical and physical properties and may also differ in biological value. An experiment in which the nutritional response to fats containing various percentages of iso-oleic acids is measured would be useful.

II. Nutritive Value of "Hard" Fats

There is still a question whether the absorption of fat from the intestine is dependent upon the "stearic acid" content of the fat, the saturated fatty acid content and/or the arrangement of the fatty acids in the triglyceride molecule. Also, it is not known whether the growth of rats is influenced by the arrangement of the fatty acids on the glycerol molecule. An investigation has been planned as an attack on this problem.

I. Dermal Absorption of Deuteriumated Soaps and Fatty Acids

Little is known of the ability of soaps or fatty acids to penetrate the dermal tissues of human beings. This subject has considerable theoretical and practical importance, and a study of the excretion of deuterium by subjects to whose skin deuteriumated compounds have been applied, would be valuable.

J. Synthesis of Glycogen from Fats

To our knowledge, no convincing experiment has yet been performed which proves the synthesis of glycogen from fats. We plan to isolate glycogen from the livers and carcasses of rats which have received deuteriumated lauric acid, and examine the glycogen for deuterium content. A "tagged" glycogen will be presumptive evidence of its synthesis from fat.

PUBLICATIONS FROM THE LABORATORIES

Reprints of publications by members of the staff of the Nutritional Biochemistry Laboratories are available to anyone requesting them. The following scientific papers were published during the period July 1, 1946 to June 30, 1948:

1. Sherman, H., M. K. Nutter, E. E. Lockhart, and R. S. Harris, "Studies on Fatty Acid Metabolism by the Deuterium Technique I. Oleic Acid." *Proc. Amer. Chem. Soc.* p. 14A, 1946.
2. Thpín, M. A., F. de P. Miranda, and R. S. Harris, "Calidad en Proteínas de Alimentos Seleccionados," *Ciencia (Mexico)* 7, 208, 1946.
3. Harris, R. S. and K. V. Thimann, "Vitamins and Hormones," Vol. IV, 406 pp., Academic Press, Inc. 1946.
4. Harris, R. S., "The Nutrition Problem of Mexico," *J. Am. Dietet. A.*, 22, 974, 1946.
5. Harris, R. S., "Essentials of a Post-War Nutrition Program," *N. Y. Legis. Doc.* 76, 48, 1946.
6. Harris, R. S., "El complejo vitamínico B en la nutrición humana." *Archivos Uruguayos de Medicina Cirugía y Especialidades* 30, 1, 1947.

NUTRITIONAL BIOCHEMISTRY LABORATORIES
DEPARTMENT OF FOOD TECHNOLOGY
MASSACHUSETTS INSTITUTE OF TECHNOLOGY
CAMBRIDGE 39. MASSACHUSETTS

March 23, 1949

ROBERT S. HARRIS, PH.D.
IN CHARGE
HAZEL E. MUNSELL, PH.D.
HENRY SHERMAN, PH.D.
LOUIS O. WILLIAMS, PH.D.
LOUISE GUILD, B.S.
ANDREW C. PEACOCK, S.M.
RITA E. BRENZ, B.S.
JUNE W. BROOIE, B.S.
LUCILLE T. KELLEY, B.S.
MERA R. JETTON, M.A.
ALINA E. SURMACKA, A.B.

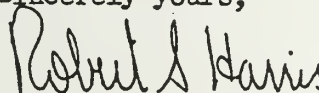
Dr. Clemens E. Benda
Medical Director
Walter Fernald School
Waverly 78, Massachusetts

Dear Dr. Benda:

I am enclosing an outline of the experiment on radioactive calcium metabolism which we discussed at luncheon last week.

After you have studied it, I wish you would telephone me so that we may discuss it and put it in final form without delay. Possibly we could schedule another luncheon with Professor Evans for Friday of this week.

Sincerely yours,



Robert S. Harris
Professor of Biochemistry
of Nutrition

RSH:im
Enclosure

NUTRITIONAL BIOCHEMISTRY LABORATORIES
 DEPARTMENT OF FOOD TECHNOLOGY
 MASSACHUSETTS INSTITUTE OF TECHNOLOGY
 CAMBRIDGE 39, MASSACHUSETTS

Wmk 7-6900

April 13, 1949

ROBERT S. HARRIS, PH.D.
 IN CHARGE
 HAZEL E. MUNSELL, PH.D.
 HENRY SHERMAN, PH.D.
 LOUIS O. WILLIAMS, PH.D.
 LOUISE GUILD, B.S.
 ANDREW C. PEACOCK, S.M.
 RITA E. BRENZ, B.S.
 JUNE W. BRODIE, B.S.
 LUCILLE T. KELLEY, B.S.
 MERA R. JETTON, M.A.
 ALINA E. SURMACKA, A.B.

Dr. Clemene E. Benda
 Medical Director
 Walter Fernald School
 Waverly 78, Mass.

Dear Dr. Benda:

I am enclosing two copies of the revised outline
 of the experiment on radioactive calcium metabolism which will
 be discussed at luncheon on Monday, the 18th, at the Hotel Puritan.

Sincerely yours,

Robert S. Harris

Robert S. Harris
 Professor of Biochemistry
 of Nutrition

RSH:im
 Enclosure(2)

*P.S. I suggest that you have it copied on your
 letterhead and have 5 copies with you at the meeting
 on Monday. RSH*

Outline of Proposed Experiment to Determine the Absorption of Calcium by Children and the Effect of Phytates upon Calcium Absorption

In this study data will be obtained on the retention of calcium by normal children and children with mental abnormalities which may affect calcium metabolism. This type of study has not been possible in the past because calcium balance studies are difficult to conduct on human subjects, are very expensive, and the results obtained are difficult to interpret. By the use of radioactive calcium, it is possible to obtain information on calcium retention promptly at little inconvenience to the subject. Since the ingested calcium has a radioactive label, an exact measurement of its excretion can be made and positive conclusions regarding its retention and excretion can be drawn from the laboratory data.

A. General Outline

Radioactive calcium (Ca^{45}) will be administered to adolescent children in the following test meals:

- Test 1. In aqueous solution in the form of calcium chloride.
- Test 2. Incorporated into a serving of oatmeal (without milk).
- Test 3. Incorporated into a serving of hydrolyzed oatmeal (without milk). The hydrolysis will destroy the natural phytic acid content.
- Test 4. In aqueous solution in the form of calcium chloride, with sodium-phytate added. The amount of phytate to equal, the phytate content of the oatmeal (Test 3).

These experiments will be performed on children whose intestinal tracts are normal. Test 1 will also include groups of mentally abnormal patients (cretins, mongoloids, those who suffer with achondralplasia and chondrolipodystrophy) whose calcium metabolism is believed to be abnormal.

By this investigation we expect to obtain the following information:

- 1. The total absorption of calcium by adolescent human subjects.
- 2. The effect of phytate in cereals (oatmeal) upon calcium absorption.
- 3. The effect of soluble phytate upon calcium absorption.
- 4. The effect of constituents of oatmeal other than phytate upon calcium absorption.
- 5. The effect of certain mental disorders upon calcium absorption.

B. Details of the Experimental Procedure

- 1. Time of Feeding. Each test feeding will be made at 7 AM in lieu of breakfast. No other food will be eaten from 7 PM of the previous evening till the noon meal on the test day. Water will be permitted except within 1 hour before and after the test feeding.

2. Amount of Calcium. Each test meal will contain 250 mg. of calcium, either in the natural food or as added calcium chloride. All calcium supplements will be fed after solution in distilled water.
3. Amount of Radioactive Calcium Fed. The amount of Ca^{45} fed in each test will be the minimum which can be used and still provide significant scientific data. No subject will receive more than 2 microcuries. A subject will be used in two test periods. If possible he will be used in more than two tests.
4. Number of Subjects. The number of normal subjects required in this study will be determined by the size of dose of radioactive calcium eventually employed. If each subject can be used in only two tests, a total of at least 20 normal subjects will be necessary. There will be no limit on the number of abnormal subjects that may be studied.

C. Preparation of Subjects for Experiment

1. Preliminary diet. During a preliminary period of 4 weeks each subject will receive a multi-vitamin supplement, also iron and an extra pint of milk daily. This should fill the calcium stores and raise all subjects to a uniform level of calcium saturation.
2. Health examination. At the beginning and end of each experiment all subjects will undergo a complete physical examination. Laboratory tests will include a complete blood analysis and serum calcium and serum phosphorus determination.

D. Preliminary Experimentation

To our knowledge this type of experiment has not been attempted by others. Though we have conducted studies on experimental animals, we do not know what proportion of the radioactive calcium ingested will appear in the urine of human subjects, nor do we know how long it will be excreted in measurable amounts. Accordingly, two subjects will be put on a preliminary test, fed one microcurie of Ca^{45} in test meal #1, and data will be obtained on the rate and amount of its excretion.

E. Supervision of Research Program

1. The subjects will be under the immediate care and supervision of Dr. Clemens E. Benda, Medical Director of the Walter Fernald School.
2. The feeding of the subjects at the Walter Fernald School and the processing of the samples will be supervised by Dr. Robert S. Harris, Professor of Biochemistry of Nutrition, Massachusetts Institute of Technology. All technical operations will be carried out by Mr. Andrew C. Peacock of his staff.

April 20, 1949

Dr. Henry A. Tadgell
Superintendent
Belchertown State School
Belchertown, Mass

Dear Dr. Tadgell:

The enclosed Research Program is a joint study between the M.I.T. and the Walter E. Fernald State School. A similar study has been done a few years ago with Dr. Cobbe when he was Assistant Superintendent at this school. The study does not include any danger to the life or health of the patient but it appears desirable to receive the official approval of Dr. Perkin's Research Committee of the Department of Mental Health of which you are chairman. Since there is interest that the preliminary steps be completed as quickly as possible, we would appreciate it if you would present the matter at the next meeting of the committee and provide an approval of the research study.

Sincerely yours,

Clemens E. Benda, M.D.
Clinical Director

CEB/P
enc.

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

DEPARTMENT OF PHYSICS

CAMBRIDGE 39, MASS.

April 26, 1949

Dr. Clemens Benda
Medical Director
Walter Fernald School
Waverly 78, Massachusetts

Dear Dr. Benda:

Enclosed are: (1) four copies of AEC Form 313 "Application for Radioisotope Procurement" made in the name of Walter Fernald School, which are complete with the exception of item 2 - Department, your signature, and the date. The original and 2 carbons of this are to go forward to the AEC, the fourth copy is for your files. (2) four copies of Form 313 made in the name of M.I.T. and already signed by Robley D. Evans. Three of these should also go forward to the AEC, the fourth again being for your files. (3) a letter from Professor Evans to Dr. Paul C. Aebersold recommending your application. This should also go to AEC with items (1) and (2).

In addition to the above three items, the following should be sent to the AEC: (1) a letter from the director of the Fernald School, giving the names of the Walter Fernald School Isotopes Committee and indicating one of these as chairman of this Committee. (2) a letter from the chairman of this Committee indicating approval for the Committee of your application.

All five documents should be addressed as indicated on the top of Form 313 and marked Attention of Dr. Paul C. Aebersold. This will complete all of the red tape with the exception of one form called Acceptance of Terms and Conditions for Order and Receipt of By-product Materials (Radioisotopes), which will be mailed to you from the AEC subsequent to the receipt of your application. If you have any questions, please don't hesitate to call on me.

Sincerely yours,


Joel B. Bulkley

JBB:m
Enclosures 9

The Commonwealth of Massachusetts
Department of Mental Health

ADVISORY COMMITTEE ON PSYCHIATRIC EDUCATION AND RESEARCH

WILLIAM MALAMUD, M.D.
 CHAIRMAN

STANLEY COBB, M.D.
 JOHN M. MURRAY, M.D.
 HARRY C. SOLOMON, M.D.

WALTER E. BARTON, M.D.
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 C. STANLEY RAYMOND, M.D.
 DOUGLAS A. THOM, M.D.

HENRY A. TADGELL, M.D.
 SECRETARY

ROY G. HOSKINS, M.D.
 DAVID ROTHSCHILD, M.D.
 JACKSON M. THOMAS, M.D.

May 7, 1949

Dr. Malcolm J. Farrell, Superintendent
 Walter E. Fernald State School
 Box C
 Waverley 78, Massachusetts

Dear Doctor:

Attn: Dr. Clemens E. Benda

At a regular meeting of this Committee held on April 27, 1949, the protocol submitted from the Walter E. Fernald State School entitled, "OUTLINE OF PROPOSED EXPERIMENT TO DETERMINE THE ABSORPTION OF CALCIUM BY CHILDREN, AND THE EFFECT OF PHYTATES UPON CALCIUM ABSORPTION" was presented. After a goodly amount of discussion, it was voted to defer approval of this project, and same will be considered again at our next meeting scheduled for June 7, 1949. Dr. Benda is invited to be present at this meeting in order to discuss any question which may arise relative to the proposed experiment. A notification card will be sent to him in due season.

Sincerely yours,

Henry A. Tadgell, M.D.
 Secretary

HAT:SS

May 18, 1949

Dr. Paul C. Aebersold
Isotopes Branch
U. S. Atomic Energy Commission
P. O. Box E
Oak Ridge, Tennessee

Dear Dr. Aebersold:

As Chairman of the Isotopes Committee, I confirm the formation of this Committee, the names of which are indicated in letter of the Director of Research. I approve of the proposed research.

Sincerely yours,

Malcolm J. Farrell, M. D.
Superintendent

MJF:may

May 18, 1949

Dr. Paul C. Aebersold
Isotopes Branch
U. S. Atomic Energy Commission
P. O. Box E
Oak Ridge, Tennessee

Dear Dr. Aebersold:

In complying with the requirements, I beg to inform you that an Isotopes Committee has been formed in order to supervise the proposed research at the Walter E. Fernald State School.

The Committee consists of the following members:

Chairman:

Malcolm J. Farrell, M. D. - Superintendent, Walter E. Fernald State School; Diplomate Board of Psychiatry.

Clemens E. Benda, M. D. - Director of Research and Clinical Psychiatrist; Diplomate Board of Psychiatry and Neurology.

Earle MacA. Chapman, M. D. - Instructor in Medicine, Harvard Medical School; Associate in Medicine, Massachusetts General Hospital.

Maximilian Weinberger, M. D. - Diplomate Board of Psychiatry; Assistant Physician, Walter E. Fernald School.

Elizabeth Belmont, M. D. - Physician, Walter E. Fernald School.

Sincerely yours,

Clemens E. Benda, M. D.

Approved:

Malcolm J. Farrell, M. D.
Superintendent

CEB:may

The Commonwealth of Massachusetts
Department of Mental Health

RECEIVED

JUN 10 1949

ADVISORY COMMITTEE ON PSYCHIATRIC EDUCATION AND RESEARCH
 Walter E. Fernald State School
 WAVERLY, MASS.

WILLIAM MALAMUD, M.D.
 CHAIRMAN
 STANLEY COBB, M.D.
 JOHN M. MURRAY, M.D.
 HARRY C. SOLOMON, M.D.

WALTER E. BARTON, M.D.
 VICE-CHAIRMAN
 GEORGE E. GARDNER, M.D.
 C. STANLEY RAYMOND, M.D.
 DOUGLAS A. THOM, M.D.

HENRY A. TADGELL, M.D.
 SECRETARY
 ROY G. HOSKINS, M.D.
 DAVID ROTHSCHILD, M.D.
 JACKSON M. THOMAS, M.D.

June 8, 1949

Dr. Malcolm J. Farrell, Superintendent
 Walter E. Fernald State School
 Waverley, Massachusetts

Dear Dr. Farrell:

Attention: Dr. Clemens E. Benda

At a regular meeting of this committee held on June 7, 1949, the conjoint protocol submitted from the Walter E. Fernald State School and the Massachusetts Institute of Technology entitled, "Outline of Proposed Experiment to Determine the Absorption of Calcium by Children and the Effect of Phytates upon Calcium Absorption", was again given consideration. I am pleased to inform you that the Committee unanimously approved of the project and we are glad that Dr. Benda could be present to answer certain questions in the minds of the members of the Committee.

Very truly yours

Henry A. Tadgell, M.D.

Secretary



UNITED STATES
ATOMIC ENERGY COMMISSION

IR:SAL

Oak Ridge, Tennessee
September 28, 1949

Dr. Clemens E. Benda
Department of Research
Walter Fernald School
Waverly 78, Massachusetts

Subject: AUTHORIZATION NO. 3435

Dear Dr. Benda:

Enclosed is Authorization No. 3435 providing for the procurement of up to three millicuries of Ca 45 of high specific activity from the Massachusetts Institute of Technology.

A carbon copy of a letter to Dr. Robley D. Evans is enclosed for your information.

We regret the delay which arose in connection with handling this application. It is improbable that similar situations would arise in the future and we can assure you that more prompt handling will be possible in case you file additional applications for isotopes. We look forward to serving your future needs for radioactive materials.

Very truly yours,



S. Allan Lough, Chief
Radioisotopes Branch
Isotopes Division
Oak Ridge Operations

Encls.:

1. Cy. ltr. fm. SAL, 9/28/49
2. Form 374, No. 3435 (in dup.)
3. Certificate, No. 3435 (in quad.)
4. Form 313, w/instructions

Form AEC-374 (Mar. 1, 1948) B. B. 38-R031.	UNITED STATES ATOMIC ENERGY COMMISSION AUTHORIZATION FOR RADIOISOTOPE PROCUREMENT	SERIAL NO. 3435
TO: Walter Fernald School Department of Research Waverly 78, Massachusetts (Attn: Dr. Clemens E. Benda)		Related to 3434 ----- DATE September 28, 1949
<p><i>The original of this form is the only approval for procurement and must accompany your purchase order. All duplicates are for informational and record purposes only.</i></p> <p><i>Your application for by-product materials is approved for the materials stated below, subject to and in accordance with your application and all laws and regulations applicable hereto.</i></p>		
1. PRICE LIST ITEM NO. H-13A	2. ELEMENT AND ISOTOPE Calcium 45	3. FORM High Specific Activity
4. TOTAL QUANTITY APPROVED Three millicuries - As requested		
5. USE OF THIS MATERIAL IS AUTHORIZED FOR THE FOLLOWING PURPOSE(S): To determine the absorption of calcium by children and the effect of phytates upon calcium absorption. Only one dose to be administered to normal children.		
6. THIS MATERIAL IS <u>IS NOT</u> AVAILABLE FROM ATOMIC ENERGY COMMISSION FACILITIES.		
THIS AUTHORIZATION EXPIRES Six months after date of issue unless extended by the Commission.	For the United States Atomic Energy Commission By <u>S. Allan Lough</u> for Chief, Isotopes Division, Oak Ridge Operations, Oak Ridge, Tennessee.	
INSTRUCTIONS TO APPLICANT		
To procure the material it is necessary that you forward the items checked below to a distributor or supplier:		
<div style="display: flex; flex-direction: column; align-items: flex-start;"> <div><input checked="" type="checkbox"/> PURCHASE ORDER FROM YOUR INSTITUTION</div> <div><input checked="" type="checkbox"/> THE <u>ORIGINAL</u> COPY OF THIS FORM (374)</div> <div><input checked="" type="checkbox"/> THREE COPIES OF THE ENCLOSED "CERTIFICATE OF COMPLIANCE WITH FEDERAL FOOD, DRUG, AND COSMETIC ACT," FORM AEC-465</div> </div>		
NOTE.—In ordering these materials from any other source address your purchase order to:	Massachusetts Institute of Technology Cambridge 39, Massachusetts (Attn: Dr. Robley D. Evans)	
INSTRUCTIONS TO SUPPLIER		
1. Advise the Isotopes Division promptly of all shipments made under this authorization.		
<p style="text-align: center;">In authorizing these materials for the uses stated in the application the Commission makes no warranty or representation that such use will not infringe any patent or patents and the authorization should not be construed as approval or acquiescence by the Commission in any infringing use of these materials.</p>		

enc 2'



Form AEC-313
(Rev. Mar. 1, 1945)

APPLICATION FOR RADIOISOTOPE PROCUREMENT

LEAVE BLANK

TO THE U. S. ATOMIC ENERGY COMMISSION, POST OFFICE BOX E, OAK RIDGE, TENNESSEE, ATTENTION: ISOTOPES DIVISION (See instructions)

1. NAME AND ADDRESS OF APPLICANT (Institution, firm, etc. See Instruction No. 2)

2. DEPARTMENT

Mass. Inst. of Tech. Cambridge 29, Mass.

Food Technology
and Physics

3. NAME AND TITLE OF SCIENTIFICALLY TRAINED INDIVIDUAL WHO WILL USE OR DIRECTLY SUPERVISE USE OF MATERIAL

Robley D. Evans, Professor of Physics

Robert S. Harris, Professor of Biochemistry of Nutrition

RADIOISOTOPE REQUESTED (See Instruction No. 3)

4. ELEMENT AND ISOTOPE

5. CHEMICAL FORM

6. QUANTITY DESIRED (Number of millicuries for separated materials, number of units for irradiated units)

Ca⁴⁵ high spec act.CaO or CaCO₃

1 irradiation unit

7. TO BE DELIVERED AT THE RATE OF (Specify quantity per week, month, etc.)

One shipment

8. CATALOG ITEM NUMBER (If material is to be acquired from a source other than AEC, omit the catalog number. Please state name and address of the person from whom material will be obtained, if known)

13A - high specific activity

STATEMENT OF USE (See Instruction No. 4)

9. STATE PROPOSED USE OF RADIO MATERIAL AND GENERAL PLAN OF INVESTIGATION

See application of Walter Fernald School. Ca⁴⁵ will be processed here for administration and samples will be measured here.

10. THE RADIOISOTOPE WILL BE USED IN HUMAN BEINGS (See Instruction No. 5)

CHECK ONE

☒ YES

NO

11. THE RADIOISOTOPE WILL BE USED IN ANIMALS (See Instruction No. 5)

CHECK ONE

YES

NO

☒

12. (To be filled out only if prior application has been filed)

CHECK ONE

YES

NO

☒

HAS THERE BEEN ANY CHANGE IN AVAILABILITY OF ITEMS CALLED FOR IN PART TWO OF THIS APPLICATION?

13. THE ISOTOPES DIVISION MAY MAKE GENERAL STATEMENTS FOR RELEASE IN THE PUBLIC PRESS REGARDING MATERIAL USED AND THE PURPOSE FOR WHICH USED

CHECK ONE

☒ YES

NO

The applicant and any official executing this application in behalf of the applicant certify that the information stated herein is true and correct and agree that The Terms and Conditions for Order and Receipt of Byproduct Materials (radioisotopes) accepted by the applicant and filed with the Atomic Energy Commission are a part hereof.

4/26/49
(Date)Robley D. Evans
(Signature of applicant or certifying official)

Section 35 (A) of the United States Criminal Code, 18 USC, Sec. 80 makes it a criminal offense to make a willfully false statement or representation to any department or agency of the United States as to any matter within its jurisdiction.



UNITED STATES
ATOMIC ENERGY COMMISSION

IR:SAL

Oak Ridge, Tennessee
September 28, 1949

Dr. Robley D. Evans
Department of Physics
Massachusetts Institute of Technology
Cambridge 39, Massachusetts

Subject: AUTHORIZATIONS NO. 3434 AND 3435

Dear Dr. Evans:

Enclosed is Authorization No. 3434 providing for procurement of three millicuries of Ca 45 in acid solution. This material will be of high specific activity and is listed as Catalog Item H-13A on page 24 of the July 1949 catalog.

We note that you have applied for one irradiated unit of Ca 45 as CaCO_3 , Catalog Item No. 13A. One irradiated unit contains about three millicuries of Ca 45. Since you specified material of high specific activity, however, we have taken the liberty of allocating the material mentioned above. It may be that you will not desire to order as much as three millicuries of Ca 45, Catalog Item No. H-13A. If a smaller amount will be adequate for your purposes, you need only to place an order for the amount really desired.

Under separate cover we have sent to Dr. Benda Authorization No. 3435 providing for procurement of the processed Ca 45 from the Massachusetts Institute of Technology. At the recommendation of our Subcommittee on Human Applications, we have stipulated that only one dose of Ca 45 is to be administered to each normal child used in the study.

We regret the delay in handling this application, which was caused by the circumstances described in Dr. Woodruff's letter to you, dated September 12, 1949, and by the necessity to resubmit the application to the Subcommittee because of differences of opinion expressed in the first review.

- 2 -

Dr. Robley D. Evans
September 28, 1949

We look forward to the opportunity to serve your future needs for radioisotopes and assure you that every effort will be made to handle your applications promptly.

Very truly yours,

S. Allan Lough, Chief
Radioisotopes Branch
Isotopes Division
Oak Ridge Operations

Encls.:

1. Form 374, No. 3434 (in dup.)
2. Certificate No. 3434 (in quad.)
3. Form 313, w/instructions

CC: Dr. Clemens E. Benda

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CITY AND STATE _____ (Print or type)

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These documents were not written for publication. They are made available in their present form, and without review by the author, only because of the urgency in releasing information to the public.

LIST NO. 14

OCTOBER 1949

BIOLOGY AND MEDICINE

AECD-51	Brookhaven Conference Report. Symposium on Radioiodine. (114 p) (1943)	\$ 1.50
MDDC-954	The Metabolism of Short-Lived Air-Borne Fission Products (39 p) (1945)	.20
MDDC-999	Effects of Single Doses of X-Rays on Rabbits (1944) (47 p)	.20
AECD-2358	A Study of the Treatment of Plutonium and Radio-yttrium Poisoning by Zirconium Citrate (12 p) (1948)	.10
AECD-2361	The in Vitro Incorporation of the Methylene Carbon Atom of Glycine into Rabbit Bone Marrow Fats (2 p) (1948)	.05
AECD-2428	Studies of the Unsaturation of Phospholipid Fatty Acids of the Liver, Kidney, and Blood of Uranium-Poisoned Rats (24 p) (1948)	.15
AECD-2447	Development of a Tissue Radiation Fluorometer (3 p) (1949)	.05

CHEMISTRY

MDDC-1228	The Absorption and Fluorescence Spectra of Bivalent Europium Ion in Crystals (10 p) (1947)	.10
MDDC-1295	The Vapor Pressure of Uranium Hexafluoride (7 p) (1947)	.10
AECD-2235	Pentavalent Manganese (5 p) (1948)	.05
AECD-2265	The System Uranyl Sulfate-Water II. Temperature-Concentration Relationships above 250°C (7 p) (1948)	.10
AECD-2342	The Spectrochemical Determination of Hafnium-Zirconium Ratios (19 p) (1948)	.10
AECD-2345	The Volatilization of BaO in the Presence of H ₂ O (3 p) (1948)	.05
AECD-2365	The Determination of Hydrogen (10 p) (1948)	.10
AECD-2370	I. The Synthesis of Toluene-1,3,5- ¹⁴ C and Oxalic Acid- ¹⁴ C from Pyruvic Acid- ¹⁴ C, II. The Mechanisms of the Reaction (11 p) (1948)	.10
AECD-2387	The Separation of Zirconium and Hafnium by Extraction with Thenoyltrifluoroacetone (5 p) (1948)	.05
AECD-2400	The Synthesis of D-Glucose-1- ¹⁴ C (87 p) (1948)	.30
AECD-2401	The Action of Aluminum Chloride of Chlorofluorocarbons (3 p) (1948)	.05
AECD-2429	Chemistry of Thorium in Aqueous Solutions. I. The Thorium-Iodate System Solubility and Complexes (19 p) (1948)	.10
AECD-2437	A Rapid Colorimetric Method for the Determination of Microquantities of Thorium (13 p) (1949)	.10
AECD-2440	Paramagnetic Susceptibilities and Electronic Structures of Aqueous Cations of Elements 92 to 95 (19 p) (1949)	.10
AECD-2443	Spectrophotometric Evidence for the Existence of Uranium Pentachloride as the Double Compound UCl ₅ ·UCl ₄ (5 p) (1949)	.05
AECD-2459	Graphical Representation of the Four Series of Isotopes (Revised) (3 p) (1949)	.10
AECD-2460	Chemistry of Aqueous Uranium (V) Solutions. I. Preparation and Properties. Analogy Between U(V), Np(V) and Pu(V) (32 p) (1949)	.15
AECD-2478	The Spectra of the Heavy elements (20 p) (1949)	.10
AECD-2523	Uranium Trifluoride - A Summary Report (7 p) (1949)	.10
AECD-2546	The Vapor Pressure of Tellurium and Selenium (Final Report) (12 p) (1948)	.10
AECD-2625	Current Radiochemical Research at Los Alamos. Proposed Talk to Be Given at Brookhaven National Laboratory (6 p) (1949)	.05
AECD-2627	A Summary of Nuclear Chemistry Work at Argonne (4 p) (1949)	.05

CHEMISTRY (cont'd)

AECD-2647	Alkaline Earth Polyuranates (6 p) (1949)	\$.05
<u>INSTRUMENTS</u>		
MDDC-544	Test of Butterfly Valve with Magnetic Transmission (14 p) (1946)	
MDDC-1495	Progress Report Low Geometry Alpha Particle Ionization Chambers (11 p) (1947)	.10
MDDC-1531	Conversion of Air Proportional Counter Alpha Detection Instruments (Poppy) to Detect C ¹⁴ Contamination and Soft Beta Radiation (4 p) (1947)	.05
MDDC-1639	Construction of a Hand-Contamination Counter and Radiation Monitor (8 p) (1947)	.10
AECD-2410	"Poppy"-Pulse Type Detector for Alphas, Betas, Gammas, and Neutrons (20 p) (1948)	.10
AECD-2535	Operations Manual for a Parallel Plate Alpha Counter (Scale of 64) (24 p) (1948)	.15

METALLURGY AND CERAMICS

MDDC-1058	High Temperature Equilibria in Metal-Metal Halide Systems (20 p) (1947)	.10
AECD-2237	Pure Refractory Materials (3 p) (1948)	.05
AECD-2464	Sintering Carbides by Means of Fugitive Binders (35 p) (1949)	.20
AECD-184	A Transient Analysis of the Cathode-Coupled Feedback Loop (26 p) (1949)	.15
MDDC-935	Studies of Capture of Gamma Rays (37 p) (1947)	.20
AECD-2250	Preliminary Results on the Cross Section of the Reaction T ³ (d,n)He ⁴ Between 1.0 Mev and 2.5 Mev Deuteron Energy (13 p) (1948)	.10
AECD-2304	Evidence for A p,d Reaction in Carbon (3 p) (1948)	.05
AECD-2340	Relative Cross Sections of Nuclear Reactions Induced by High Energy Neutrons in Light Elements (8 p) (1948)	.10
AECD-2368	Graphs Showing Neutron Cross Sections as Functions of A, Z, or N (8 p) (1948)	.10
AECD-2382	Alpha Particles From Fission as Recorded by Photographic Emulsions (11 p) (1948)	.10
AECD-2438	On the Derivation and Integration of the Pile-Kinetic Equations (17 p) (1949)	.10
AECD-2449	Slowing Down on Neutrons in Polychrystalline Solids (10 p) (1949)	.10
AECD-2533	Inelastic Scattering of Lead for 14.5 MEV Neutrons (4 p) (1949)	.05
AECD-2569	Energy Loss of Deuterons in D ₂ O at very Low Energies (20 p) (1949)	.10
AECD-2585	Half-Life of Tritium (9 p) (1949)	.10
AECD-2641	Conductivity Changes in Dielectrics During 2.5 MEV X-Radiation (3 p) (1949)	.05
AECD-2664	Neutron Physics (96 p) (1945)	.35

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UNITED STATES
ATOMIC ENERGY COMMISSION

IR:SAL

Oak Ridge, Tennessee
September 28, 1949

Dr. Robley D. Evans
Department of Physics
Massachusetts Institute of Technology
Cambridge 39, Massachusetts

Subject: AUTHORIZATIONS NO. 3434 AND 3435

Dear Dr. Evans:

Enclosed is Authorization No. 3434 providing for procurement of three millicuries of Ca 45 in acid solution. This material will be of high specific activity and is listed as Catalog Item H-13A on page 24 of the July 1949 catalog.

We note that you have applied for one irradiated unit of Ca 45 as CaCO_3 , Catalog Item No. 13A. One irradiated unit contains about three millicuries of Ca 45. Since you specified material of high specific activity, however, we have taken the liberty of allocating the material mentioned above. It may be that you will not desire to order as much as three millicuries of Ca 45, Catalog Item No. H-13A. If a smaller amount will be adequate for your purposes, you need only to place an order for the amount really desired.

Under separate cover we have sent to Dr. Benda Authorization No. 3435 providing for procurement of the processed Ca 45 from the Massachusetts Institute of Technology. At the recommendation of our Subcommittee on Human Applications, we have stipulated that only one dose of Ca 45 is to be administered to each normal child used in the study.

We regret the delay in handling this application, which was caused by the circumstances described in Dr. Woodruff's letter to you, dated September 12, 1949, and by the necessity to resubmit the application to the Subcommittee because of differences of opinion expressed in the first review.

- 2 -

Dr. Robley D. Evans
September 28, 1949

We look forward to the opportunity to serve your future needs for radioisotopes and assure you that every effort will be made to handle your applications promptly.

Very truly yours,

S. Allan Lough, Chief
Radioisotopes Branch
Isotopes Division
Oak Ridge Operations

Encls.:

1. Form 374, No. 3434 (in dup.)
2. Certificate No. 3434 (in quad.)
3. Form 313, w/instructions

CC: Dr. Clemens E. Benda

October 27, 1949

S. Allan Lough, Chief
Radioisotopes Branch
Isotopes Division
Oak Ridge Operations
Oak Ridge, Tennessee

Dear Mr. Lough:

We confirm the authorization of the United States Atomic Energy Commission for the use of three millicuries of $\text{Ca } 45$ to determine the absorption of calcium by children.

The authorization, Serial Number 3435, states: "Only one dose to be administered to normal children." The interpretation of this statement by the physicist is that one dose means the physical unit of three millicuries which could, however, be given for instance in three fractions of one millicurie each time at various intervals.

Will you please be good enough to confirm this interpretation or otherwise correct it.

Sincerely yours,

Clemens E. Benda, M. D.
Clinical Director

Approved:

Malcolm J. Farrell, M. D.
Superintendent.

CEB:may



*copy to
Mr. Harlow*

UNITED STATES
ATOMIC ENERGY COMMISSION

IR:JRM

Oak Ridge, Tennessee
November 3, 1949

Dr. Clemens E. Benda
Walter E. Fernald State School
Box C
Waverley 78, Massachusetts

Subject: AUTHORIZATION NO. 3435

Dear Dr. Benda:

This office is pleased to reply to your letter of October 27 regarding the dosage restriction placed on Authorization No. 3435 by our Subcommittee on Human Applications.

Only one dose to be administered to normal children was meant to indicate that each normal patient used in your study would receive radiocalcium one time only.

There also appears to be some misinterpretation of the authorized dosage. Your letter of October 27 states "the interpretation of this statement by the physicist is that one dose means the physical unit of three millicuries which could, however, be given, for instance, in three fractions of one millicurie each time at various intervals." It should be pointed out that 3 mc is the total activity authorized for your program. The individual dosage was approved for the amount shown in the outline attached to your Application No. 3435. This was:

"3. Amount of Radioactive Calcium fed. The amount of Ca 45 fed in each test will be the minimum which can be used and still provide significant scientific data. No subject will receive more than 1 microcurie. A subject will be used in two test periods. If possible he will be used in more than two tests".

To summarize, you are authorized to conduct your investigation as you originally requested using the minimum amount of Ca 45 which would provide significant scientific data in each test. Mentally deficient subjects may be used in more than one test providing the total Ca 45 administered per subject does not exceed one microcurie. The Subcommittee on Human Applications further recommended that normal control subjects be used in one test only with the minimum possible Ca 45 and in no case to exceed one microcurie.

- 2 -

Dr. Clemens E. Benda
November 3, 1949

We trust these arrangements are satisfactory for the conduct of your investigation. If we can be of further assistance, feel free to call on us.

Very truly yours,

James R. Mason
for S. Allan Lough, Chief
Radioisotopes Branch
Isotopes Division
Oak Ridge Operations





MALCOLM J. FARRELL, M. D.
SUPERINTENDENT

The Commonwealth of Massachusetts
Department of Mental Health

WALTER E. FERNALD STATE SCHOOL
BOX C, WAVERLEY 78, MASS.

November 2, 1949

The Massachusetts Institute of Technology and this institution are very much interested in the various aspects of nutrition, particularly how the body absorbs various cereals, iron and vitamins.

We are considering the selection of a group of our brighter patients, including..... to receive a special diet rich in the above mentioned substances for a period of time. We wish to keep an accurate record of the effect of these substances, such as, gains in weight and other improvements, particularly in the blood. It will be necessary to make some blood tests at stated intervals, similar to those to which our patients are already accustomed, and which will cause no discomfort or change in their physical condition other than possibly improvement. The Massachusetts Institute of Technology plans to reward patients taking part.

Enclosed please find a blank which I request that you sign and return in the enclosed stamped addressed envelope, as soon as possible. The signed and witnessed blank will signify that you have no objection to your son participating in this project as outlined above.

You may rest assured that I personally feel this project will be of great importance and that much valuable information concerning nutrition can be obtained which eventually will be of considerable benefit to mankind. I hope that I can count on your cooperation.

Very truly yours,

MJF:d
Enclo.

Malcolm J. Farrell, M.D.,
Superintendent.



TO THE SUPERINTENDENT OF THE
WALTER E. FERNALD STATE SCHOOL:

This is to state that I give my permission for the participation of
_____ in the project mentioned in your letter of

Witnessed by:

Signature

Date:

Relationship

TO THE SUPERINTENDENT OF THE
WALTER E. FERNALD STATE SCHOOL:

This is to state that I give my permission for the participation of
_____ in the project mentioned in your letter of

Witnessed by:

Signature

Date:

Relationship

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WALTER E. FERNALD STATE SCHOOL:

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_____ in the project mentioned in your letter of

Witnessed by:

Signature

Date:

Relationship



NUTRITIONAL BIOCHEMISTRY LABORATORIES
DEPARTMENT OF FOOD TECHNOLOGY
MASSACHUSETTS INSTITUTE OF TECHNOLOGY
CAMBRIDGE 39, MASSACHUSETTS

RECEIVED
JAN 15 1950

Walter E. Fernald State School
WAVERLY, MASS.

March 10, 1950

ROBERT S. HARRIS, PH.D.
IN CHARGE
HAZEL E. MUNSELL, PH.D.
HENRY SHERMAN, PH.D.
LOUIS O. WILLIAMS, PH.D.
LOUISE P. GUILD, B.S.
RITA E. BRENZ, J.S.
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MERA R. JETTON, M.A.
ALINA S. SZCZESNIAK, A.B.
ANN McNALLY, A.B.
CHARLOTTE F. BELSER, B.S.

Dr. Malcolm Farrell
Fernald State School
Waverly, Massachusetts

Dear Dr. Farrell:

During the period January 24 through January 30, 1950 we collected slurries of food being served at the Fernald School and analyzed it for the nutrient value.

The samples collected on each day were studied for thiamine, riboflavin, niacin and ascorbic acid content and the results were as follows:

Table A:

	<u>Thiamine</u>	<u>Riboflavin</u>	<u>Niacin</u>	<u>Ascorbic Acid</u>
	mg.	mg.	mg.	mg.
Jan. 24	1.181	1.511	14.15	96.0
" 25	1.418	1.572	8.45	86.5
" 26	1.536	1.771	14.95	93.9
" 27	1.042	2.636	10.09	180.4
" 28	1.144	1.817	13.33	93.2
" 29	1.201	1.656	19.13	110.2
" 30	1.280	1.856	13.24	93.4
Average	1.25	1.831	13.33	107.1

A composite of samples collected over the entire 7 day period was analyzed for these and other nutrients with the following results:

-2-

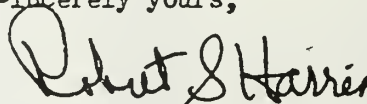
Table BResults for Composite for Seven Days

<u>Constituent</u>	<u>Amounts* per day</u>	<u>N. R. C. Allowance 12-15 year old boy</u>
Moisture	2244.7 gm	-
Ether extract	86.0 "	-
Crude fiber	3.2 "	-
Nitrogen	15.2 "	12.8 gm
Ash	23.6 "	-
Calcium	1017.0 mg	1300 mg
Phosphorus	1800.0 "	1850 mg
Iron	25.3 "	15. mg
Carotene	3.18 "	5000 IU
Thiamine	1.29 "	1.5 mg
Riboflavin	1.83 "	2.0 mg
Niacin	13.50 "	15.0 mg
Ascorbic acid	108.8 "	190.0 mg

*This was calculated on the basis of average weight of food for the seven days.

In Table B we have listed the recommended dietary allowance of children as set up by Food and Nutrition Board of the National Research Council. You will note that the food being served at the Fernald School does pretty well in meeting these estimated requirements.

Sincerely yours,



Robert S. Harris
Professor of Biochemistry
of Nutrition

RSI:im

MASSACHUSETTS INSTITUTE OF TECHNOLOGY
CAMBRIDGE, MASS.

DEPARTMENT OF FOOD TECHNOLOGY

May 1, 1953

3118
3126 - 2118
B. E. PROCTOR — Professor of Food Technology
Head of Department
R. S. HARRIS
Professor of Biochemistry of Nutrition
C. G. DUNN
Associate Professor of Industrial Microbiology
E. E. LOCKHART
Associate Professor of Food Chemistry
H. SHERMAN
Assistant Professor of Biochemistry of Nutrition
J. T. R. NICKERSON
Assistant Professor of Food Processing
S. A. GOLDBLITH
Assistant Professor of Food Technology

Dr. Clemens E. Benda
Director of Research
Walter E. Fernald State School
Waverley 78, Massachusetts

Dear Dr. Benda:

As you know, we are planning to conduct a study to measure the availabilities of different calcium compounds in human subjects. In order for this study of five different calcium sources to be studied properly, we have planned an experimental design which will require fifteen subjects.

On May 29th Dr. Bronner spoke with Dr. Kelly regarding the subjects and he stated that as of that time he had ten subjects lined up. On May 1st he indicated that three of these subjects objected to be included in the study and this reduced the number to seven.

However, Dr. Kelly stated that five of the subjects ^{which} had previously received 1 microcurie of radiocalcium were willing to be used in this experiment. While we are delighted that these boys are willing, they will not be as satisfactory as fresh subjects because they have already received some calcium and we cannot give them 5 microcuries more. According to our experimental design, each subject will receive 1 microcurie on each of five experimental tests.

We sincerely believe that this study is of very great clinical importance. We therefore hope that you will do everything possible to help us obtain a proper number of subjects for this experiment. It seems to me that the three subjects who objected to being included in the study can be induced to change their minds.

It has been our experience that we need to round up about seventeen subjects if we hope to use fifteen in an experiment. If there is anything I can

-2-

do to help in this please let me know. For instance, it occurs to me we have neglected the Fernald Science Club angle of our work and should line up a baseball game for the boys. Possibly it would be worthwhile for us to arrange an assembly so that we could tell the boys something about our work and get them to feel satisfied their small pain is really worthwhile.

Sincerely yours,

Robert S Harris

Robert S. Harris

RSH:im

May 3, 1953

53

St Binda

Colonial Director 1/2 Mrs S. Willis

Dear Doctor -

The following boys at the Boys Home have signified their willingness to participate in the new scientific test by M. I. T. :-

- 1- [REDACTED]
- 2- [REDACTED]
- 3- [REDACTED]
- 4- [REDACTED]
- 5- [REDACTED]
- 6- [REDACTED]
- 7- [REDACTED]

Additionally the following boys at Boys Home who have previously been in the science tests are willing to participate again if accepted :-

- 1- [REDACTED]
- 2- [REDACTED]
- 3- [REDACTED]
- 4- [REDACTED]
- 5- [REDACTED]

The doctor in charge at M. I. T. has been advised as above. For other boys are available at the Boys Home or Boys Territory.

As previously should not the parents or guardians be written by you for their consent, as the boys are all feeble minded minors, before authorization by the Dept for the proposed tests.

[Copy to be Communicated next. Dept.]

S. Willis

May 28, 1953

Dear Parent:

In previous years we have done some examinations in connection with the nutritional department of the Massachusetts Institute of Technology, with the purpose of helping to improve the nutrition of our children and to help them in general more efficiently than before.

For the checking up of the children, we occasionally need to take some blood samples, which are then analyzed. The blood samples are taken after one test meal which consists of a special breakfast containing a certain amount of calcium. We have asked for volunteers to give a sample of blood once a month for three months, and your son has agreed to volunteer because the boys who belong to this Science Club have many additional privileges. They get a quart of milk daily during that time, and are taken to a baseball game, to the beach and to some outside dinners and they enjoy it greatly.

I hope that you have no objection that your son is voluntarily participating in this study. The first study will start on Monday, June 8th, and if you have not expressed any objections we will assume that your son may participate.

Sincerely yours,

Clemens E. Benda, M.D.
Clinical Director

Approved:

Malcolm J. Farrell, M.D.
Superintendent

CEB/dfg

SCIENCE CLUB BOYS - BH 6/5/53

9 AM. 1/21/54
no breakfast 1/21/54

(permission received June, 1953)

(permission from father 11/6/49)

1/25/54 ✓

1/21/54 ✓

1/21/54

1/25/54 ✓

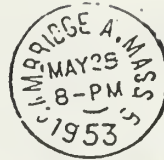
1/25/54

WARD 22 6/5/53 (Dr. Weinberger over phone)

	Born	Mental age	IQ	Weight
1/25/54	1940	80	71	116 lbs.
Term 1/25/54 Bk	1940	82	55	140 lbs.
	1940	72	59	112 lbs.

X ray.

PLEASE 3 DAYS RETURN TO
BOX C
WAVERLEY 78, MASS



B-24/A
WISE
U.S.S

REASON CHECKED
Undelivered.....
Unknown.....
For better address.....
Moved, Left no address.....
No such office in town.....

Mass.

NOTE

THEY
KEPT
RETURNED
ENVELOPES
TO SHOW
ATTEMPT
TO
DELIVER

AND
LISTED
OUT
KNOWN
RELATIVES

- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED] - mother
- [REDACTED] - father
- [REDACTED] - mother
- [REDACTED] - mother
- [REDACTED] address
- [REDACTED] - Grandmother Mrs. [REDACTED]
- [REDACTED] no address
- [REDACTED] (mother)
- [REDACTED] (father)

Not delivered
W/ [REDACTED]
b/ [REDACTED]

(*) LIST
OF
STUDENTS
LETTERS WENT
OUT TO PARENTS
OF

June 29, 1953

Mrs. [REDACTED]

[REDACTED] Massachusetts

Dear Mrs. [REDACTED]:

We have heard that you plan to take your son [REDACTED] on vacation on July 1st. [REDACTED] is cooperating in a science test and it is extremely important that he be here on the 1st and 2nd of July. Will you be good enough to change the beginning of [REDACTED] vacation from Wednesday, July 1st, to Friday, July 3rd?

If for any reason unknown to us this is not possible, please call me or my secretary at Waltham 5-3600 immediately after receiving this letter.

Thanking you,

Sincerely yours,

Clemens E. Benda, M.D.
Clinical Director

Approved:

Malcolm J. Farrell, M.D.
Superintendent

CEB/dfg

ANNUAL REPORT
OF THE
RESEARCH LABORATORY
WALTER E. FERNALD STATE SCHOOL
WAVERLEY 78, MASSACHUSETTS
July, 1952 - June, 1953

The research activities of the Department covered a larger field of investigations than in previous years, due to the fact that more and more research has been done along clinical and biological lines in connection with different research departments in the Boston area.

The main research at the Department of the Walter E. Fernald School is still centered around research in neuropathology of mental disorders. There were 15 autopsies performed between July 1, 1952, and June 30, 1953. These 15 autopsies out of 30 deaths represent a percentage of 50 per cent, which appears quite satisfactory. The material of these autopsies was prepared for microscopic study, and in many instances hundreds of serial sections were made to have a complete picture of the underlying pathology and, at the same time, satisfactory material for teaching purposes.

It is interesting to note that in contrast to previous years, only one mongoloid was among these cases whereas 4 cases were hydrocephalics, 3 microcephalics, and the others mainly cases of brain injury with different forms of brain damage and cerebral palsy.

The material on hydrocephaly was worked up and partly used in a presentation given at the meeting of the American Association of Neuropathologists in Atlantic City on June 14, 1953. The title of the paper was: "The Dandy-Walker Syndrome or the So-called Atresia of the Foramen Magendie." This paper will be published in a memorial issue for the late Dr. Joseph Globus which will be issued by the Journal of Neuropathology and Experimental Neurology, probably in January, 1954.

Research in mongolism has been continued and new results have been presented at a Symposium on Mongolism held at the Jewish Hospital in Brooklyn, New York, on February 27th. This paper has been published in the May issue

-2-

of the QUARTERLY REVIEW OF PEDIATRICS under the title, "Research in Congenital Acromicria (Mongolism) and its Treatment."

The research in mongolism moved from neuropathological research to biochemical research. A study of the protein-bound-iodide in mongolism is at present carried out in cooperation with the Massachusetts General Hospital, Thyroid Laboratory. These studies are of extreme significance in order to gain more insight into the function of the thyroid in mongolism. At the same time, a number of patients have been studied with I^{131} at the Thyroid Laboratory of the Beth Israel Hospital, in order to study the up-take of the thyroid.

In order to get more insight into adrenal and pituitary function, a study of eosinophilic reactions was carried out, mainly by Dr. Bowman with the assistance of Mr. ~~W. W. W.~~, making eosinophilic counts in mongoloids before and after application of ACTH and adrenalin. The result of this study is included in the publication, "Research in Congenital Acromicria (Mongolism) and its Treatment."

Another line of investigation is being done with Dr. George Mann of the Harvard School of Public Health, Department of Food Research, to determine cholesterol molecules which have been reported as abnormal by Dr. John Gofman and his co-workers at the meeting of the American Psychiatric Association in Los Angeles, California, May 8, 1953. This paper was discussed by Dr. Benda and Dr. Farrell at that meeting, Dr. Farrell presenting the discussion. Our own studies concerning the different cholesterol molecules were carried out in a way that the blood of 21 mongoloids and 21 control cases, matched by chronological and mental ages, was sent in to Dr. Mann's laboratory without attached diagnosis and the blood was analyzed in order to see whether significant differences could be detected. In this study, mongoloids of an age

-3-

between 16 and 30 were studied because we considered it of interest to see whether there is an inherent metabolic disturbance present in mongolism which would appear in the fat metabolism even in younger age groups. The preliminary results of this study seem to indicate that this is not so. There may, however, be an inherent tendency to abnormal metabolism which becomes more and more obvious as age progresses, and we shall now study an older age group to see whether significant changes will occur with increased age, which would, of course, be also a result of extreme importance.

Another line of investigations is proceeding with regard to calcium metabolism. This research is carried out with the Department of Food Technology at the Massachusetts Institute of Technology under the direction of Professor Robert S. Harris and a coordinating investigator, Dr. Felix Bronner. In this study, different calcium preparations and types of meals are used to study the calcium absorption from food by means of Ca^{45} . These studies are of great interest for many reasons. Calcium metabolism is still fairly unknown and the ways of absorption, storage and excretion are only insufficiently established. The present study promises to permit a set of very definite scientific data which will settle a number of arguments.

Another experimental study is carried out with feeding and mating experiments on rats and mice, which are fed with food deficient in certain properties. The animals are observed clinically in developing certain deficiency symptoms, and a number of them are then sacrificed and studied anatomically. Some of the surviving animals have been used for mating experiments because the anatomical studies have shown definite evidence that the gonadal system is very susceptible to deficiency diseases and abnormal sperm cells occur readily. For the field of mental deficiency, it is therefore of great interest to study whether the offspring of food-deficient animals shows a higher percentage of malformations

-4-

and fetal deaths. As far as the present study goes, the data at hand seem to prove this point.

Teaching and educational activities at the Research Department have increased steadily during the last year, and the load of teaching obligations has been increasingly felt.

During the past year the National Institute of Mental Health has continued the grant for training in psychiatry, which position was filled by Dr. Peter W. Bowman. Dr. Bowman spent most of his time at the Research Laboratory, participating actively in the research, and in the Outpatient Clinic.

There have been a great many visitors to the Research Department, who wanted to see what kind of research is done in mental deficiency and to learn about the basic facts.

The Staff of the Research Laboratory consists of the following:

The secretary, Mrs. ~~XXXXX~~, who has done a great amount of work beyond the usual capacities of one secretary so that it was not necessary to engage a part-time second secretary during the last year, as has been done in previous years. On account of her unusual efficiency, it was voted in March, 1953, to augment her salary by an additional \$10 a month, to make up at least partly the difference between her salary as a State employee and the salary of a Federal secretary which had been offered her on different occasions.

The Tissue Laboratory employs Mrs. ~~XXXXX~~ and Miss ~~XXXXX~~. Mrs. ~~XXXXX~~ has been shifted to the State employee roll and receives, therefore, only a small additional sum to make up for the salary to which she would be entitled according to her long years of service and efficiency. The salary of Miss ~~XXXXX~~ has been increased after a year of service at the Research Laboratory.

September 29, 1953

Atomic Energy Commission
Isotopes Division
P.O. Box 8
Oak Ridge,
Tennessee

Attention: Sub-Committee on Human Applications

Gentlemen:

This letter is written in order to elicit your permission to administer a dose of 50 mc Ca^{45} to a moribund gargoyles patient now hospitalized in our institution.

Diagnosis: Gargoylism (Chondrolipodystrophy).
(See Clemens E. Banda: DEVELOPMENTAL DISORDERS OF MENTATION
AND CEREBRAL PALSIES, 1952, Grune & Stratton, New York.)

The patient is a child of 6 years, suffering from this severe metabolic disorder since birth but going progressively downhill at present. There is no doubt about the diagnosis, which is confirmed by clinical studies and x-ray studies. Children who develop this metabolic disorder early in life usually die before they reach an age of 10 and not more than 15 years. This patient has had an especially severe condition for the last year, and his life expectancy is now limited to a few months. For this reason I respectfully urge prompt consideration of this application. It will be appreciated if you will notify me at once if this request cannot be acted upon promptly.

I have been conducting studies on the Ca^{45} metabolism of mentally deficient patients in cooperation with Drs. R. S. Harris and F. Bronner of the Massachusetts Institute of Technology for the past 3½ years. Permission for the use of small quantities of radiocalcium is contained in Authorization No. 13974, dated May 8, 1952, and Authorization No. 18444, dated March 10, 1953.

Permission for the use of higher doses administered to moribund patients has been granted by you to other investigators, as evidenced by the report of Ballin and Lasalo (Science, 117,331-4, 1953.)

In view of the foregoing it is my hope that you will consider this request favorably.

Respectfully yours,

Clemens E. Banda, M.D.
Director of Research and
Clinical Psychiatry

CEB/dfg

October 6, 1953

[REDACTED]
Boston, Mass. (Apartment [REDACTED])

Dear Mrs. [REDACTED]:

We cannot find that we have ever received a reply to our letter of August 7th, asking permission for your son to participate in examinations in connection with the nutritional department of the Massachusetts Institute of Technology. As stated in that letter, the tests are made for the purpose of improving the nutrition of our children and, in general, to help them more efficiently than before.

[REDACTED] has expressed willingness to participate in this project and we would greatly appreciate it if you would sign the enclosed permission and return it at your earliest convenience.

Sincerely yours,

Clemens E. Benda, M.D.
Director of Research and
Clinical Psychiatry

Approved: Malcolm J. Farrell, M.D.
Superintendent

CEB/dfg
Enclosure

MASSACHUSETTS INSTITUTE OF TECHNOLOGY
CAMBRIDGE, MASS.

DEPARTMENT OF FOOD TECHNOLOGY

B. E. PROCTOR — Professor of Food Technology
Head of Department
R. S. HARRIS
Professor of Biochemistry of Nutrition
C. G. DUNN
Associate Professor of Industrial Microbiology
E. E. LOCKHART
Associate Professor of Food Chemistry
H. SHERMAN
Assistant Professor of Biochemistry of Nutrition
J. T. R. NICKERSON
Assistant Professor of Food Processing
S. A. GOLDBLITH
Assistant Professor of Food Technology

December 2, 1953

RECEIVED

DEC 3 - 1953

Walter E. Fernald State School
WAVERTLEY, MASS.

Dr. Malcolm T. Farrell, Superintendent
Walter E. Fernald State School
Waverley, Massachusetts

Dear Dr. Farrell:

As in the past years, we again would like to give a Christmas party to the boys of the Science Club who cooperated with us during 1953. We have arranged for a dinner party to be held at the M.I.T. Faculty Club, 50 Memorial Drive, Cambridge, at 5:30 P.M. on Wednesday, December 16, 1953. We would very much like to have you, Dr. Benda, and Dr. Kreplick join us in this festivity.

For your convenience we are enclosing a list of the boys who participated in the studies this past year. We would appreciate your letting us know at an early date whether the date suggested is convenient, whether all of the boys will be able to come, and how many attendants will accompany them.

There is ample parking space in the back of the Faculty Club, off Madsworth Street. The Club is located on the sixth floor but one of us will meet the group on the ground floor.

Cordially yours,

Robert S. Harris

Robert S. Harris

Felix Bronner

Felix Bronner, Ph.D.
Research Associate

RSH im
Enclosure

33 letters sent

10/21/55 dated 10/18/55

- 1.) [redacted] (father) ✓
- 2.) [redacted] (mother) ✓
- 3.) [redacted] (Adopted Mother) ✓
- 4.) [redacted] (fa) ✓
- 5.) [redacted] (mo) ✓
- 6.) [redacted] (mo) ✓
- 7.) [redacted] (parents) ✓
- 8.) [redacted] (per) ✓
- 9.) [redacted] (mo) ✓ Mrs. [redacted]
- 10.) [redacted] (mo) ✓
- 11.) [redacted] (father mo) ✓
- 12.) [redacted] (mo relatives) ✓
- 13.) [redacted] (mo) ✓ Mrs. [redacted]
- 14.) [redacted] (sister) miss [redacted] ✓
- 15.) [redacted] (parents) ✓
- 16.) [redacted] (mo) ✓
- 17.) [redacted] (aunt) Not a parent. ✓
- 18.) [redacted] (Parents) ✓
- 19.) [redacted] (family) ✓
- 20.) [redacted] (mo) ✓
- 21.) [redacted] (mo) ✓ Mrs. [redacted]
- 22.) [redacted] (mo) ✓ Mrs. [redacted]
- 23.) [redacted] (parents) ✓
- 24.) [redacted] (father) ✓
- 25.) [redacted] (father/mother) Mr. & Mrs. [redacted] ✓

- 26) ✓ [redacted] (Aunt) Mrs [redacted]
- 27) [redacted] (No add. since 1951)
- 28) [redacted] (for) ✓
- 29) [redacted] (Mother)
- 30) [redacted] (Mo)
- 31) [redacted] (parents)
- 32) [redacted] (parents)
- 33) ✓ [redacted] (Mo)
- 34) ✓ [redacted] (grandfather) letters sent from parent
- 35) [redacted] (No add.) odd.
- 36) [redacted] (to add.) since (1947) to address
- 37) [redacted] (Foster Mother) [redacted] fathers letter [redacted] 1943



MALCOLM J. FARRELL, M. D.
SUPERINTENDENT

The Commonwealth of Massachusetts
Department of Mental Health

WALTER E. FERNALD STATE SCHOOL

BOX C, WAVERLEY 78, MASS.

October 18, 1955

Dear Miss [REDACTED]:

We wrote to you on September 12th about some planned research in conjunction with the Nutritional Department of the Massachusetts Institute of Technology, and asked that you sign the permission slip for the participation of your son in this project.

Most of the parents have given permission for their sons to participate, and we would appreciate receiving definite answer, either "yes" or "no", since the studies ~~are~~ going to be started soon.

Sincerely yours,

Clemens E. Benda, M.D.
Clemens E. Benda, M.D.
Clinical Director

Approved: *Malcolm J. Farrell*
Malcolm J. Farrell, M.D.
Superintendent

CEB/dlg



The Commonwealth of Massachusetts
Department of Mental Health

15 ASHBURTON PLACE, BOSTON 8

JUN 5 - 1956

RECEIVED
 L. Frank Spaulding
 WAVERLY, MASS.

June 1, 1956

FROM: Commissioner
 TO: Superintendent

Dear Doctor:

The Governor and some members of the Legislature expressed interest in the kinds of research going on in our institutions. Since it has been approximately 18 months since we conducted such a round-up I would like to have the following information within the next ten days:

A paragraph, not more, on each research project in your place. The paragraph should contain the following information. The kind of project, for example, biochemical studies in schizophrenia, with a statement whether it involves protean or other factors or another example might be sociologic studies on the role of _____ and _____. I should like to know approximately the number of persons involved in it and the number of patients involved. A brief statement as to about when this project will be completed and the hypothesis being tested. I don't want a detailed report of the progress of the study I only want to know what's going on and what its general purposes are. I believe this will prove advantageous to us in structuring next years budget.

Sincerely yours,

Jack R. Evalt
 Jack R. Evalt, M. D.
 Commissioner

JRE:MIM

The Task Force to Review Human Subject Research

Massachusetts Department of Mental Retardation

January 24, 1994

Frederick M. Misilo, Jr., Esq.
Chairperson

Doe West
*Project Coordinator
& Archivist*

Task Force Members

Dr. Marylou Buyse

Dr. Allen Crocker

Prof. Gunnar Dybwad

Dr. Anne Howard

Richard Krant, Esq.

Doris Manson

Rep. Edward Markey

George Mavridis

Dr. Philip Reilly

Rev. Richard Robison

Virginia Tisci, Esq.

David W. White-Lief, Esq.

RE: Human Subjects Testing and Research on the
Mentally Retarded

Dear

Philip Campbell, Commissioner of the Massachusetts Department of Mental Retardation, has established a Task Force to Review Human Subject Research. I am writing to you today on behalf of the Task Force to request certain information which may be in the possession of your institution.

The Task Force is charged with the following: To review and report on any and all research projects which utilized radioactive and other potentially harmful material involving human subjects within the facilities for the mentally retarded operated by the Commonwealth of Massachusetts. To that end, we are asking your institution, along with several others in Massachusetts, and along with several divisions of the state government, to supply certain information on human subjects testing. We are asking for your cooperation, recognizing that collecting such information is a difficult and time-consuming task, especially given that some of the research in question took place decades ago. At the same time, we will need your promptest possible attention to our request for information, so we can proceed with our task as quickly and efficiently as possible.

In order to limit the inquiry to a more manageable time period, we are seeking information on human subjects testing at all of the State School which conducted between 1943 and 1973. For the purposes of this inquiry, we are limiting the terms "testing" and "research" to include testing on human subjects which included the use of radioactive materials, and/or testing which included the introduction of any harmful or potentially harmful compound into a human subject. This inquiry specifically excludes noninvasive behavioral research at this time, although the Task Force may later extend its inquiry into this area.

TASK FORCE TO REVIEW HUMAN SUBJECT RESEARCH

January 24, 1994

Page 2

We ask that you construe this definition broadly, and that you include in any answer projects funded by your institution, projects conducted under the auspices of your institution, and/or any projects of which you are aware which were conducted by any employee of your institution, under the supervision of any employee, and/or by or in connection with any faculty, student, fellow, or volunteer. Should you discover additional research projects conducted between 1943 and 1973 which do not fall within the definition above, but which involved individuals with mental retardation, please identify them for us in any case.

"State School" includes any one of (or any combination of) the following: Walter E. Fernald State School in Waltham; the former Belchertown State School, the Wrentham State School in Wrentham; the Glavin Regional Center in Shrewsbury; the Paul A. Dever State School in Taunton; the Hogan/Berry Regional Center in Hathorne; the Monson Developmental Center in Monson; and the Templeton Developmental Center in Baldwinville.

In your initial inquiry, we ask you to focus on studies involving radioactive materials. We ask that you provide the Task Force with copies of documents in your institution's custody that appear to have been generated in connection with any of the following types of research believed to have taken place:

--The actual or proposed use of radioactive iron in research involving residents of the Fernald State School;

--The actual or proposed use of radioactive calcium in research involving residents of the Fernald State School;

--The actual or proposed use of radioactive iodine in research involving residents of the Fernald State School.

We certainly understand that when reviewing records from this long ago, you will find that the data is often primitive and/or that the records may be scattered through a number of places or even intermingled in personal collections. However, in order to complete this inquiry in a way that truly allows accurate information to be given to potential subjects, we must ask that you undertake the same intensive and extensive review that all involved institutions and agencies are conducting. Specifically, the type of information we ask that you identify and provide includes the following:

1. **Identify Research Projects.** Please identify all research projects that were conducted by your institution at the State Schools for the period 1943 to 1973. Please include in your answer the name of the project, state the dates the project began and ended, and state the purpose(s) of the project.

2. **Identify Researchers.** For each project identified in your answer to Question 1, please identify each person who directed, conducted, and/or participated in the project.

TASK FORCE TO REVIEW HUMAN SUBJECT RESEARCH

January 24, 1994

Page 3

3. **Identify Human Subjects.** For each project identified in your answer to Question 1, please identify each human subject who participated in the project. If the names of the subjects are not known, which we have found to be common, please provide any other available identifying data, such as date of birth, social security number, or residence.

4. **Describe the Research Methodology.** Please describe in reasonable detail how each human subject was utilized in each project identified in your answer to Question 1. Please describe the data collected and the results of the study.

5. **Identify Publications.** If any of the projects identified in your answer to Question 1 was the subject of a scientific publication or was the subject of a thesis or dissertation, and the paper, please provide us with a copy of the document, regardless of whether it was published in the scientific literature. If you do not have a copy of the document, please provide an appropriate reference to the document, and identify any person known to be in possession of the document so we may retrieve a copy.

6. **Consent.** The Task Force is closely evaluating the question of informed consent in connection with human subjects research. With regard to each project identified in your answer to Question 1, please state whether consent was sought and/or obtained for the study, and if so, from whom. Please describe how consent was obtained, and identify any documents which reflect the consent obtained. If you locate consent forms, please send us copies of them.

7. **Identify Funding Sources.** It would greatly assist the Task Force if you would identify the source of any funding for the research you identify and describe. This will enable the Task Force to conduct follow-up investigation through additional sources.

As you conduct this investigation into your archives, kindly copy materials for our task force which relate to your answers to the questions above. We would appreciate receiving all documents which describe any research conducted, and especially any documents which identify human subjects. We would also appreciate receiving copies of any other documents identified in response to any of the questions above.

As the Task Force has been given a deadline of March 31, 1994 to complete its investigation, time is of the essence. **We ask that your reply to these requests be delivered on or before February 9, 1994.** To the extent that we are able to identify additional specific research projects which took place at the State Schools, we will notify you as quickly as possible. Also, it would greatly assist the Task Force if your institution would designate one person at your institution who will serve as our primary contact person for the purposes of this request for information.

We understand that these requests may require considerable effort on the part of your institution. Be assured that we are not asking you to do

TASK FORCE TO REVIEW HUMAN SUBJECT RESEARCH

January 24, 1994

Page 4

anything we have not already asked certain State agencies to do as well. If you are unable to complete this investigation within the time allotted, please provide as much preliminary information as possible by February 9, 1994. The questions are set forth in order of the Task Force's priorities.

Please be advised that your responses to these questions will be a matter of public record, except where your responses identify human subjects, in which case appropriate confidentiality will be maintained. If you would like advice or direction in undertaking this review, please call Doe West at (617) 894-3600 Extension 2582 for further instructions *prior to the deadline of February 9, 1994.*

Finally we want to emphasize our desire to work cooperatively with your institution and others. We greatly appreciate your assistance in helping to bring relevant information to our attention in a timely and orderly way.

Please direct all questions about this letter, as well as all responses, to:

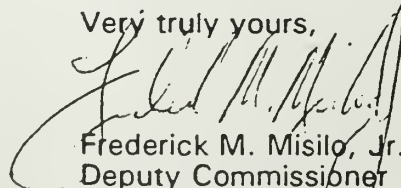
Doe West
Project Coordinator
Task Force to Review Human Subject Research
c/o Fernald State School
P.O. Box 9108
Belmont, MA 01278

Hand deliveries may be made as follows:

Doe West
Project Coordinator
Task Force to Review Human Subject Research
Howe Library
Fernald State School
200 Trapelo Road
Waltham, MA

Thank you very much for your anticipated cooperation.

Very truly yours,



Frederick M. Misilo, Jr.
Deputy Commissioner
Chairman, Task Force to Review
Human Subject Research

cc: Philip Campbell, Commissioner
Task Force Members

**INDIVIDUALS REQUESTED TO PROVIDE INFORMATION
ON HUMAN SUBJECTS TESTING**

Each of the following persons was contacted in February, 1994, and asked to provide comprehensive information to the Task Force concerning human subjects testing at the State Schools between 1943 and 1973. The full text of the letter sent is appended hereto:

Mitchell T. Rabkin, M.D.
President
Beth Israel Hospital
330 Brookline Avenue
Boston, MA 02215

J. Robert Buchanan, M.D.
General Director
Massachusetts General Hospital
55 Fruit Street
Boston, MA 02114

✱ Lewis W. Pollack
Superintendent
Boston City Hospital
818 Harrison Avenue
Boston, MA 02118

John H. Britt
Superintendent
Massachusetts Hospital School
3 Randolph Street
Canton, MA 02021

H. Richard Nesson, M.D.
President
Brigham & Women's Hospital
75 Francis Street
Boston, MA 02115

✱ Elizabeth Coniaris
Chief Executive Officer
Massachusetts Mental Health Center
74 Fenwood Road
Boston, MA 02115

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On Human Subjects Testing
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STATE FACILITY REVIEW REPORT FROM THE METHODOLOGY SUBCOMMITTEE

File reviews and interviews were conducted by staff at state facilities to identify additional studies or experiments which utilized radioactive materials during the 1943 to 1973 periods. No such experiments or studies were identified. (As noted below, independent sources identified experiments at the Fernald and Wrentham State Schools).

At the Walter E. Fernald State School, based on data received from outside sources and reported in scientific journals, identities of some resident participants were established.

At the Wrentham State School, again based on information from independent outside sources and scientific journals, experiments were identified, some positive identification of participants was made. The medical files of identified and possible participants of the Wrentham studies (1962) were examined and none contained data indicating participation or consent to participate.

8,000 to 10,000 medical files of former residents of Fernald State School alone are located in facility and state archives. No attempt was made by the Task Force to review all of these files as our experience had been that resident medical files do not (except in rare instances) contain data concerning radioactive material experiments. (This information was kept separately by researchers and not otherwise recorded at the state facilities).

We consulted with two medical statisticians:

■ Dr. Monroe G. Sirken,
Associate Director for Research and Methodology
National Center for Health Statistics, U.S. Dept. of Health and Human Services

■ Dr. Nancy Veeder
Associate Professor, Graduate School of Social Work
Boston College

Both statistical experts suggested that a random sampling search of archival medical files would not be productive in view of our experience that files do not contain notations of radioactive experiments.

Set forth below are synopses of searches conducted at the various facilities. Detailed reports of their efforts are contained in the appendix.

1. BELCHERTOWN STATE SCHOOL (now closed)

Staff of the Monson Developmental Center contacted Dr. Aaron Kasparian, Medical Director 1964-1985. He advised that no experimental research was done at Belchertown during the period he was there.

Dr. Kasparian noted that Dr. Bowser was the Superintendent in 1964 and had been there approximately 20 years. Dr. Bowser never mentioned any kind of experimentation or research to Dr. Kasparian. Dr. Kasparian never saw any notations in medical records indicating experimental treatments.

Annual reports also reviewed by staff:
Board of Trustees (1923 to 1992)
Board of Trustees minutes of meetings
(1923 to 1992)
Human Rights Committee files
(1981 to 1992)
Superintendent's files
(1976 to 1993)

2. PAUL A. DEVER STATE SCHOOL

Contacted former employees, searched archival material, reviewed minutes of Board of Trustees meetings and

Board of Trustees annual reports. Provided a list of present and past Superintendents and Medical Directors. Reviewed in detail medical records of current residents who were living at Dever when Fernald experiments were conducted.

3. WALTER E. FERNALD STATE SCHOOL

Archival material housed in the Howe Library was searched by staff for any mention of research, experiments or other accounts dealing with radioactive materials. Included were: monthly reports from the Research Unit of Fernald, Superintendent's Reports, the correspondence of Superintendents and Clinical Directors, Annual Reports and boxes of miscellaneous material.

The initial review of archival records (client records and medical records) began with the names found on the "Christmas Club" list identified in the press. Thereafter, every time a list of names was found in materials from Fernald's archives, or submitted in papers supplied by Harvard and M.I.T., those records were retrieved and reviewed.

Persons calling the "800" phone line or sending a letter that involved a male who was here in the correct time frame also triggered an archival review.

The most extensive sources, submitted to us, were files and reports, which had been donated by individuals to universities. We also performed extensive reviews of medical literature of the day for further clues on studies and subjects.

Reviews of the medical files of the 74 individuals identified by name as subjects of studies failed to disclose a single reference to radiation experiments.

4. GLAVIN REGIONAL CENTER

Staff reviewed medical records for indications of any forms of medical experiments. Interviewed medical staff, reviewed Human Rights Committee files. Provided list of medical directors and Superintendents.

5. HOGAN/BERRY REGIONAL CENTER

Staff reviewed facility records and archival material. Interviewed staff and concluded that there had been no active medical research at this facility.

6. MONSON DEVELOPMENTAL CENTER

Staff reviewed historical files (that date back to the late 1800's). Interviewed nursing supervisor (1950's to 1980's). Provided list of medical directors and Superintendents.

7. TEMPLETON DEVELOPMENTAL CENTER

(formerly a unit of the Fernald State School)

Staff interviewed:

- former Superintendent and wife (1952 to 1977)
- former unit supervisor (1957 to 1981)
- former recreation supervisor (1962 to 1991)
- another unit supervisor (1950 to 1982)
- former senior L.P.N. (1952 to 1983)

8. WRENTHAM STATE SCHOOL

Staff reviewed Trustees minutes 1933 to 1965; located Wrentham State School Article List - with data re: 18 articles published 1910 to 1955 by staff members. Completed a 10% random sampling including records of 20 current and 20 deceased/discharged former residents. Reviewed 500 to 600 publications in record room. Using data from the same "Pediatrics" article identified 61 residents who were between ages 1 and 16 at any time between 1960 and 1965. Medical records of all of these persons were examined in archives and no

evidence of "thyroid study" was located.

A second level of review was conducted by the Project Coordinator Doe West, Chairperson Frederick Misilo and Task Force Member Richard Robinson. They were able to match records with birthyears and gender to positively identify twelve persons. This will be ongoing as the working group now focuses on the Thyroid studies over the summer of 1994.

DMR Task Force on Human Subject Experimentation
CONTACT WITH SUBJECTS & INQUIRIES SUBCOMMITTEE
February 28, 1994 (Revised March 4, 1994)

Subcommittee Report

A meeting was held with members of the Fernald Social Work Department, as well as members of the Wrentham State School Social Work Department, to discuss the status of communication with experiment "subjects" and plan for further contact with these individuals. Doe West and Rich Robison also participated in the meeting. This report summarizes issues discussed at that meeting. Issues raised in subsequent conversations with Dr. Allen Crocker and Dr. Gunnar Dybwad have also been incorporated into this report. Preliminary Subcommittee recommendations, discussed during all previous meetings, are also included.

Status of Communications with Involved Individuals

To this date, no communication has been **initiated** with the individuals believed to have been involved in "radiation experiments". Communication has been only with those who have self-identified through the "800 number" and with interested individuals who have called the 800 number.

- ◆ There have been approximately 300 calls to the "800 number" at Fernald State School.
- ◆ To date, it has been determined that approximately 74 "science club members" participated in experiments involving radiation.
- ◆ Only 10 of these 74 participants have been located through the process of calling the "800 number". An additional two individuals have been identified, but **62 known participants have still not identified themselves to the Department.** [Note: On 3/4, Rich Robison found that it may be possible to locate an additional 9 or 10 individuals as a result of their continuing involvement with DMR. The numbers in the remainder of this document do not reflect this new finding.]

ISSUE: What efforts should be taken to find the 62 individuals from Fernald known to have participated in the radiation experiments?

Doe outlined potential avenues for finding the involved individuals through public information channels. These include identification by the Department of Revenue, the Department of Corrections, and Social Security. In many cases, our efforts are hindered by the fact that we don't have Social Security numbers for the participants. A letter to Senator Kennedy's Office asking for assistance in obtaining Social Security numbers has not received a response. None of these individuals currently reside at Fernald, and two of them are believed to be dead, but this has not been confirmed.

The group discussed both formal and informal methods for finding the 62 known Science Club participants in the experiments:

Formal Efforts - Options for formal efforts included the use of a state agency (e.g., Department of Revenue, Department of Public Safety), or retaining a private agency. (A Maryland based agency specializing in "detective work" associated with medical cases has been identified. The cost of using such an agency has not been determined. [Allen Crocker subsequently suggested that the current DMR client list be reviewed to determine if any of these individuals are known to DMR.]

Informal Efforts - It was suggested that we request the 12 known participants (including Task Force Members Austin & Charlie) to assist the Department through "networking" to obtain the addresses of as many of the remaining 62 as possible. The possibility of bringing together known participants for a meeting was discussed. This type of gathering would facilitate peer support, allow contact with Fernald Social Services staff, and might facilitate the location of other participants. [Subsequently, Allen Crocker strongly endorsed this idea.]

Other informal strategies mentioned included contacting potential past or present employers (e.g., Waltham Ladder), and contacting physicians and clergy in areas believed to be the most likely residence of experiment participants (e.g., Lowell, Waltham).

Discussion - After considering these options for identifying experiment participants, the group began discussing the more critical issue of **obligation to inform versus respecting participant's privacy**. For example, if we recommended that a state or private agency be charged with "tracking down" these 62 participants, might we also run the risk of "making public" some information about these individuals that had been intentionally kept private? Austin and Charlie shared their experiences of having gone public with the fact that they once lived at Fernald State School. It was suggested that additional efforts be made to publicize the Task Force's and the Department's work on this issue so that additional participants might voluntarily identify themselves. (Gerry Ryan, DMR spokesperson, may be able to provide assistance in this area.)

Fernald Social Service personnel explained the process being used to review records and document findings on an Archive Retrieval Form. The question was raised as to whether this process was yielding all of the information that would be useful in finding the individual. For example, one Social Worker reported that he was recording the names and birth dates of all known siblings. It was suggested that a public or private agency with experience locating "missing" individuals be asked, "What information would be most useful to obtain from individual's record for subsequent use in locating that individual?"

This discussion led us to the more basic question of **What benefit is there for the individual who chooses to come forward, or who is identified through formal or informal methods?** If medical experts suggest that providing a medical examination and ongoing monitoring will have a high probability of preventing future health problems, then

the obligation to inform could override the concern for respecting an individual's privacy. On the other hand, if it is highly unlikely that medical examination or monitoring will result in significant benefit to the individual, then the individual's privacy should be a higher priority.

The group meeting on 2/25 agreed that a "reasonable effort" should be made to locate experiment participants, but that each individual's privacy should be a prime consideration. Further, the extent of the efforts to find individuals should be impacted by the information provided by medical experts and legal opinion on this question. We were left with the question of **What constitutes "reasonable effort" to locate experiment participants?** The Task Force may need additional expert opinion to answer this question.

ISSUE: Once an experiment participant has been located, through formal or informal methods, what is the best method of communicating with him about his participation in the experiments?

Due to the sensitive nature of this information and the potential for misunderstanding written material, it was generally agreed that once additional experiment participants have been identified, initial communication should take place in person, or via telephone if face-to-face contact is not possible. Subsequent communication should be done by telephone. In all instances, written material should be sent concurrently for review by the individual and his family if desired.

PRELIMINARY RECOMMENDATIONS

- (1) Former residents of Fernald State School (or their family members) who have called the 800 number, and who we now believe not to have participated in any of the major studies (n=approx. 300) should be contacted as soon as possible with this information. They should also be told that they will be contacted again if any new information pertaining to participation by them becomes available. This information should be communicated by telephone with a letter sent concurrently.
- (2) As soon as medical expert opinion has been received, all known experiment participants (n=12) should be invited to a "gathering" at the Fernald State School, or at another location preferred by the participants. The purposes of this gathering would be to facilitate communication in a supportive atmosphere, allow for peer support, allow contact with Fernald Social Work staff, and to aid in the location of other participants.

- (3) Once additional experiment participants have been located, initial communication should take place in person, or if face-to-face contact is not possible, it should be done via a "careful" telephone conversation. Written materials should be provided concurrently.
- (4) To facilitate ongoing communication with experiment participants, a "sole correspondent" should be identified for each participant. This individual should have ongoing access to up-to-date information about risks as well as available resources for health and mental health services. Toll-free access should be maintained.
- (5) For persons without access to mental health services, DMR should explore options for counseling, including, but not be limited to, the Department of Mental Health.
- (6) If an experiment participant does not have health insurance, DMR should provide assistance to facilitate linkage with an existing resource for medical care coverage (e.g., MassHealth). If it is not possible to access financial coverage through traditional channels, DMR should arrange for access to and payment for health care services.

*** The scope of coverage for medical follow-up should be discussed by the Task Force after we have received the opinions of medical experts. Dr. Crocker also raised an important question about what is being done for persons without mental retardation who received "comparable" radiation exposure. If this information is not already available to the Task Force, it should be acquired.

- (7) A packet of information should be developed for experiment participants to share with their physicians. This material should include information pertaining to radiation exposure and potential implications for health care.

Anne M. Howard

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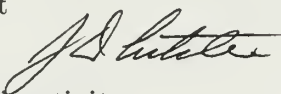


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April 9, 1994

To: Reverend Doe West
From: J. David Litster 
Subject: Radiation and Radioactivity

Here is a brief introduction to some of the terms and ideas used to discuss radioactivity and radiation, which I hope some readers of your report may find useful.

What is Radiation?

The kind of radiation we are concerned with is called "ionizing radiation", which interacts with matter to produce charged ions by separating electrons from the atoms. The ions can cause chemical changes in tissue, such as modifying the DNA in cells, which may result in long term health consequences. The radiation must have enough energy to make ions. Radio waves, microwaves, and light are forms of electromagnetic radiation which do not have enough energy to produce ions. X-rays and gamma-rays are higher energy forms of electromagnetic radiation which do produce ions.

Commonly, ionizing radiation is produced by the decay of unstable (radioactive) nuclei. In addition to x-rays and gamma-rays, they can produce beta-rays (high energy electrons), alpha-particles (high energy helium nuclei), protons, and neutrons.

How is Radioactivity Measured?

The amount of radioactive material is measured in units of *curies*, abbreviated Ci. A curie is enough material to produce 370 billion (3.7×10^{10}) radioactive decays per second; that is the number produced by one gram of radium. Another unit of activity is the *becquerel*, which is one decay per second.

The amount of radiation absorbed by matter can be described by saying how much *energy* the matter has absorbed. A common unit is the *rad*, which means that one cubic centimeter has absorbed one erg of energy. An erg is a very small amount of energy. (It takes about 42 million ergs to increase the temperature of one cubic centimeter of water by one degree centigrade.) The radiation dose received by an organ, such as the thyroid gland, is usually expressed in rads¹.

¹Modern writers may use the approved international unit called the *gray*. One gray equals 100 rads.

What is the Biological Effect of Radiation?

If we want to compare the biological effect of exposure to different amounts and kinds of ionizing radiation, we need to know what is called the whole body effective dose equivalent. That is expressed in terms of a unit called the *rem*, which stands for "roentgen equivalent man"². To calculate the effective dose equivalent, the dose of radiation to different organs (bone marrow, lungs, thyroid, etc.) is multiplied by a factor corresponding to the biological effectiveness of the type of radiation. These effective doses for all the organs are multiplied by a weighting factor for each organ and added together. The resulting number, in rems or sieverts, is a measure of the risk of the radiation. All effective dose equivalents which have the same number of rems or sieverts are presumed to pose the same risk of harmful effects, no matter what the source of radiation or what organs received the radiation.

As Dr. James Adelstein explains in his letter of March 24, 1994, high doses of radiation (hundreds of rems) can have two kinds of biological effects in humans and animals. These effects appear shortly after exposure to the radiation, and may be repaired with time. With the studies at the Massachusetts State Schools, we need be concerned only with low doses of radiation (measured in millirems³) which have, if any, only delayed effects.

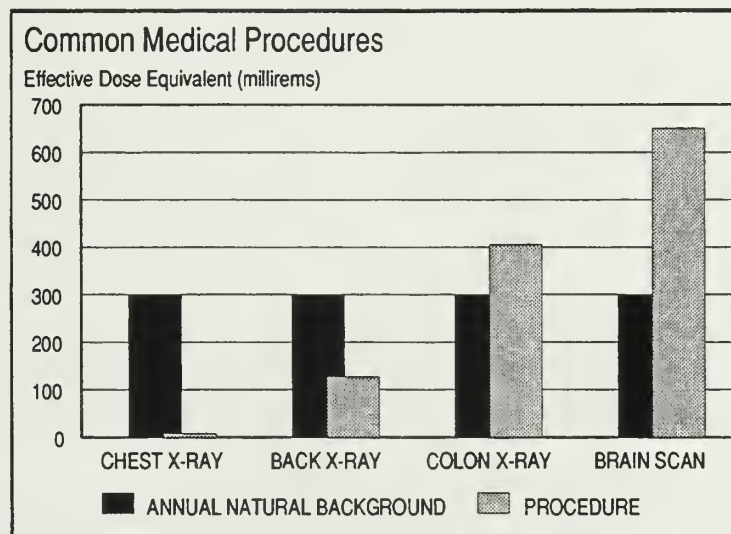
The delayed effects of low doses of radiation are of two kinds: increased incidence of cancer, and an increase in genetic defects. Dr. Adelstein's letter gives the current (conservative) estimates for what these delayed effects may be. In some cases, such as exposure of the thyroid to radiation from iodine-131, large scale epidemiological studies have been made⁴, and we have a reasonably good idea of the delayed effects of low doses. Some scholars feel that where iodine-131 is concerned, the effective dose equivalent overestimates the risk by three times. In other situations, we can use the general risk factor proposed by the National Council on Radiation Protection and Measurements, which is that a 1000 millirem exposure carries an increased risk of 5 additional cancers per 10,000 individuals exposed.

²Modern writers may use the approved international unit called the *sievert*. One sievert equals 100 rems.

³1 millirem is 1/1000 rem, or 1/100000 sievert.

⁴L.-E. Holm, K.E. Wiklund, G.E. Lundel, N.A. Bergman, G. Bjelkengren, U.C. Ericsson, E.S. Cedergren, M.E. Lidberg, R.S. Lidberg, H.V. Wicklund, and J.D. Boice, Jr., "Cancer Risk in Population Examined with Doses of ¹³¹I", *J. Nat. Cancer Inst.* 81, 302-306 (1989).

The whole body effective dose equivalent for some common medical procedures is shown in the graph below, along side the annual 300 millirem natural background effective dose equivalent which is received by residents of the Boston area.





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A PRIMER ON RADIATION

Radiation Comes from Cosmos, Our Bodies; How Much Radiation Is Considered Safe?

Editor's Note: The table below compares 1. the radiation exposures to the whole body which are the established Federal standard for various activities (Note: The first Federal standard for fetuses of pregnant radiation workers went into effect yesterday.); 2. amounts of natural background radiation; 3. common sources of additional radiation; 4. amounts from medical treatment (very high radiation to a limited part of the body); and 5. amounts from diagnostic research (low levels from radioactive tracer elements). The source of this information is Francis Masse, director of the Radiation Protection Office of the Massachusetts Institute of Technology. Masse is a past president of the Health Physics Society and served in 1987-89 as chairman of the National Academy of Sciences panel which reviewed the exposure of soldiers to radiation from atmospheric testing in the 1940s and 1950s.

ASTRONAUTS: 25,000 MILLIREMS PER SHUTTLE MISSION

The highest recommended limit for radiation exposures is for astronauts-- 25,000 milliRms per Space Shuttle mission, principally from cosmic rays. This amount is beyond the average 300+ milliRms of natural sources of radiation and any medical radiation a person has received.

25,000 milliRms per year was the Federal occupational limit during World War II and until about 1950 for radiation workers and soldiers exposed to radiation. The occupational limit became 15,000 milliRms per year around 1950. In 1957, the occupational limit was lowered to a maximum of 5,000 milliRms per year.

AVERAGE NATURAL BACKGROUND: 300 MILLIREMS PER YEAR

The average exposure in the United States, from natural sources of radiation (mostly cosmic radiation and radon), is 300 milliRms per year at sea level. Radiation exposure is slightly higher at higher elevations--thus the exposure in Denver averages 400 milliRms per year.

(A milliRem is 1/1000th of a Rem. According to McGraw-Hill's Dictionary of Scientific and Technical Terms, a Rem is a unit of ionizing radiation equal to the amount that produces the same damage to humans as one roentgen of high-voltage x-rays. The name is derived from "Roentgen equivalent man." Wilhelm Roentgen discovered ionizing radiation in 1895 at about the same time that Pierre and Marie Curie discovered radium.)

All of these limits are for the amount of radiation exposure in addition to background radiation and medical radiation.

ADULT: 5,000 MILLIREMS PER YEAR

The current Federal occupational limit of exposure per year for an adult (the limit for a worker using radiation) is "as low as reasonably achievable; however, not to exceed 5,000 milliRms" above the 300+ milliRms of natural sources of radiation and any medical radiation. Radiation workers wear badges made of photographic film which indicate the exposure to radiation. Readings typically are taken monthly. A Federal advisory committee recommends that the

(MORE)

lifetime exposure be limited to a person's age multiplied by 1,000 milliRems (example: for a 65-year-old person, 65,000 milliRems).

MINOR: 500 MILLIREMS PER YEAR

The maximum permissible exposure for a minor under 18 working with radiation is one-tenth the adult limit or not to exceed 500 milliRems per year above the 300+ milliRems of natural sources, plus medical radiation. This was established in 1957 and reviewed as recently as 1990.

FETUS: 500 MILLIREMS OR 50 PER MONTH (NEW RULE JAN. 1)

New federal regulations went into effect New Year's Day, establishing for the first time an exposure limit for the embryo or fetus of a pregnant woman exposed to radiation at work. The limit for the gestation period is 500 milliRems, with a recommendation that the exposure of a fetus be no more than 50 milliRems per month.

WEIGHT VARIABLES

Like alcohol intoxication levels, levels of exposure to radioactivity (due to radioactivity deposited in the body) depend on a person's weight. A diagnostic tracer of one micro Curie of radioactive calcium 45, given orally, would result in an exposure of 3.7 milliRems for a 100 pound person, and half of that, 1.85 milliRems, for a 200 pound person.

THERAPEUTIC RADIATION

Therapeutic radiation treatment that is delivered by administering radioactive material via the mouth or by injection usually results in high, very localized doses to a small part of the body, which absorbs most of the radioactivity. The radioactivity concentrates and remains in the target organ (example: the thyroid) for a longer period of time than does the radioactivity that is distributed to the rest of the body. The radiation exposure for other parts of the body is a function of the amount of radioactivity per pound and the time the radioactivity is present in the tissue.

GEORGE BUSH'S HYPERTHYROID PROBLEM

For example, a hyperthyroid problem such as that experienced by former President George Bush is typically treated with a radioactive iodine drink designed to deliver about 10,000,000 milliRems of radioactive iodine to the thyroid. It would coincidentally deliver a dose to the rest of the body of about 20,000 milliRems. Another example, using a slightly lower dose of radioactivity, is used for cancerous tumors. A radiation dose to kill a cancerous tumor often sends a radiation beam delivering 6,000,000 milliRems to the cancerous tissue, but the whole body equivalent dose is much less, as it was in the thyroid example cited above.

What is a lethal dose from a single instance of radioactivity? According to studies made after the atomic bomb explosions in 1945 at Hiroshima and Nagasaki, half of the people died whose entire bodies were exposed to 450,000 milliRems of radioactivity from the atomic bomb. All persons died whose bodies were exposed to 600,000 milliRems of radioactivity.

See Table, Next Page.

Federal Standards, Permissible Levels Of Radiation Exposure to Whole Body (1994 unless noted otherwise)

MilliRems Above Natural Background Levels (Average 300) and Medical Radiation

- +25,000** Astronauts, per Space Shuttle mission. *This also was the annual occupational limit for adults from World War II through 1950.*
- +15,000** *1950 to 1957 Occupational limit per year for adults, including radiation workers and soldiers. Limit changed in 1957 to +5,000 milliRems.*
- +5,000** (Since 1957) Occupational limit per year for adult radiation workers, including soldiers exposed to radiation. It is "as low as reasonably achievable; however, not to exceed 5,000 milliRems." It is recommended that lifetime cumulative exposure is not to exceed the age multiplied by 1,000 milliRems.
- +500** Occupational limit per year for a minor under 18 years of age exposed to radiation. An embryo or a fetus of a pregnant worker exposed to radiation (a new regulation as of Jan. 1, 1994) is not to exceed more than 500 cumulated total milliRems before birth, and it is recommended that the exposure of a fetus be limited to no more than about +50 milliRems per month.

Sources of Naturally-Occurring Radiation

(Whole Body Equivalents)

- 25 to 35** Human body's own radiation dose per year from radioactive elements and minerals in the body.
- 300** Average annual natural background radiation, sea level (includes your own body radiation, cosmic radiation and radon).
- 400** The city of Denver's average annual natural background radiation (altitude 5,000 feet).

Common Additional Sources of Radiation

(Whole Body Equivalents)

- +12** Coast-to-coast U.S. round trip flight in airplane at 35,000 feet of altitude.
- +10** Annual increase due to daily use of salt substitute (potassium chloride) or eating a diet heavy in such potassium-rich foods as bananas and Brazil nuts. Potassium is an essential dietary element that is present mostly in the muscles.
- +2** Annual exposure due to watching four hours of television every day.

Therapeutic Doses of Radiation to A Part of the Body

(Whole Body Equivalents)

- +20,000** Therapeutic radioactive iodine treatment of thyroid gland. A localized dose delivers 10,000,000 milliRems to the thyroid, and about 20,000 milliRems to the rest of the body. A radiation dose to kill a cancerous tumor often sends a radiation beam delivering 6,000,000 milliRems to the cancerous tissue, but the whole body equivalent dose is much less, as in the thyroid case.

Doses of Radiation for Medical Diagnosis or Research Purposes (Whole Body Equivalents)

- +500 to
+200 Cardiac stress test.
- +245 Exposure of one 70 pound youth in Federal research at the Fernald School by MIT in the 1940s, using trace elements to track iron absorption while eating cereal. The research showed iron supplements should not be taken with meals.
- +172 Average exposure of 17 youths, ages 12 to 17, avg. weight 100 lbs., in the above research.
- +127 Exposure of heaviest youth, 135 lbs., in the above research.
- +2 to +7 Exposure received by 45 youths, ages 10 to 16, in Federal research in the 1950s by the Fernald School, with the assistance of MIT. The study used radioactive calcium 45 to track calcium absorption. One adult (age 21) received a higher dose, resulting in an exposure equal to 11 milliRems for the whole body.
- +2 One Chest X-ray (the whole body equivalent). A typical X-ray exposes the chest to a dose equal to 20 milliRems at the entrance and 1 milliRem at the exit. Averaging this exposure over the whole body yields a whole body equivalent of about 2 milliRems.

The U.S. Food & Drug Administration's current regulations state,

"The amount of radioactive material to be administered shall be such that the subject receives the smallest radiation dose with which it is practical to perform the study without jeopardizing the benefits to be obtained by the study. Under no circumstances may the radiation dose to any adult research subject from a single study, or cumulatively from a number of studies conducted within one year, be generally recognized as safe if such doses exceed the following:

Single dose for an adult 3,000 milliRems

Annual total dose 5,000 milliRems

For a research subject under 18 years of age at the last birthday, the radiation dose shall not exceed 10% of that set forth above."

Therefore, the single exposure limit for a child is 300 milliRems (whole body equivalent) and the annual total exposure cannot exceed 500 milliRems.

Since 1968, medical researchers at the institution doing the research have been required to follow informed consent procedures. These procedures require the assent (if feasible) of a child 7 years of age or older, and the consent of both parents if there is any perceived risk involved in the research. For research involving any perceived risk, there also has to be a relationship between the study and a child's disorder or disease.

If there is direct benefit that is likely to accrue from participation in the study, then a researcher needs the assent of the child (age 7 or older) and the consent of at least one of the parents. In such direct benefit research situations, the permitted levels of radiation can be exceeded.

END

KDC/FM 1/2/94



Testimony on MIT Nutrition Research Involving Radioactive Tracers and Human Subjects

J. David Litster

MIT

Fernald School

January 13, 1994

My name is David Litster and I am a Professor of Physics and Vice President and Dean for Research at MIT. My own field of research is condensed matter physics, so I am not an expert on health physics. However, I have learned a lot about the subject in the past two weeks, and I am accompanied by our Radiation Protection Officer, Mr. Francis X. Masse, who will answer any questions that are too difficult for me.

I am here to tell you how the Massachusetts Institute of Technology has responded to the recent series of newspaper stories. These stories concerned research with human subjects in the 1940s and 1950s in which radioactive materials were used and which involved MIT faculty, staff, or students.

I first became aware of the research when an article appeared in the Boston Globe on December 26. The next day I began to make some phone calls to determine what was behind the stories, and later that day MIT President Charles M. Vest asked me to supervise a review of the issues. The aims of that review have been to understand:

- The nature, purpose, and results of the research.
- The amount of radiation the subjects were exposed to, and the levels of risk that it presented according to both 1950s understanding and current knowledge.
- Any information which might help to identify the subjects, in order that it might be communicated to the Massachusetts DMR Task Force.

- Institute policies regarding the use of human subjects in experiments which existed at the time, and a comparison with current Institute policies.

President Vest has expressed his concern over the apparent lack of fully informed consent involved in nutritional research conducted by MIT at the Walter E. Fernald School, and issued the following statement to the press:

"I was sorry to hear that at least some of the young people who participated in this research and their parents apparently were unaware that the study involved radioactive tracers. People should not unknowingly become the subjects of research studies of this type. We have had in place for more than two decades at MIT numerous safeguards and approval processes that assure informed consent of human subjects of any research. It is important to recognize that the purpose of these studies was to improve understanding of nutritional processes in order to promote health of young people, and that radiation exposure appears to have been well within even today's limits."

We have started to examine the archival records at MIT in order to learn as much as we can about these matters. I have essentially completed a review of the nutrition research using Fernald School pupils which was conducted by MIT Professor of Nutrition Robert S. Harris in the late 1940s and early 1950s. This research required the addition of minute amounts (less than one billionth of an ounce) of radioactive iron or calcium to breakfast cereal eaten by the participants, in order to trace how iron and calcium were absorbed from their diet, and in particular to determine how chemicals naturally present in some cereals would affect the uptake of these minerals from the diet.

The research was published in four scientific papers that are listed in the appendix to these notes.

I would like to share a summary of my findings with you today. These findings are from the scientific publications based on this research, a reading of the Ph.D. Thesis of Felix Bronner, which was based on the calcium studies, a conversation with Dr. Bronner, and

several discussions with Dr. Constantine Maletskos, a co-investigator in the research. Frank Masse has instructed me on matters of the effective dose of radioactive materials and the risks involved.

What was the Research About?

The purpose of the research was to understand how the body obtained the minerals iron and calcium from dietary sources and to find out whether chemical compounds naturally present in certain cereals, such as rolled oats, affected their absorption.

Use of Iron Tracer: One of the scientific articles contains the results of a series of studies using radioactive iron as a tracer, carried out over a year in the late 1940s; 17 youths from the Fernald School were involved. Earlier studies on the nutritional value of bread had shown that certain chemicals, known as phytates, could inhibit the uptake of dietary iron. These investigations showed that rolled oats, which do contain phytates, did not reduce iron uptake from the diet when compared to farina (e.g., Cream of Wheat)—which does not contain phytates. Professor Harris' research also showed that adding phytates in soluble form to the diet reduced the iron absorption 15-fold, and that both the oatmeal and farina breakfasts alone reduced it about 3-fold. The general conclusion was that iron supplements to the diet should not be given with meals. In addition, children living in institutions could continue to eat oatmeal—which many of them probably did in large amounts—without concern for negative dietary effects, so far as iron uptake was concerned.

Use of Calcium Tracer: These studies were carried out in the 1950s to determine the effect of these same phytate chemicals on calcium absorption from the diet. This time subjects were fed oatmeal and farina breakfasts and the milk contained a minute amount of radioactive calcium (about two trillionths of an ounce) as a tracer to monitor the absorption of calcium by the body. The subjects were 36 youths aged 10 to 17 from the Fernald School, and each received two breakfasts three weeks apart containing radioactive calcium tracer. The conclusion was that if the oatmeal were accompanied by sufficient milk, the phytates in oatmeal had no effect on the amount of calcium absorbed by the body. They also showed that if only about two ounces of milk were given, the farina breakfast permitted better

absorption of the calcium in the milk. Most American diets were found to contain enough calcium that the phytates in food do not pose a problem for calcium absorption.

A third set of studies involved the direct injection of small amounts of radioactive calcium. The subjects were nine youths from the Fernald School, aged 11 to 15, and one adult. The purpose of these studies was to determine what happened to calcium once it entered the blood stream (they showed it goes quickly to the bones) and also to see if calcium present in the feces contributed to the body's calcium balance. That knowledge is essential for metabolic studies involving calcium. The conclusion was that the body excretes calcium mostly through the urine, with only about a third being excreted in the feces. The studies also showed that the body excretes injected calcium very slowly. This research using radioactive calcium tracers to understand calcium metabolism laid the foundation for much subsequent research on osteoporosis.

How Much Radiation Did The Subjects Get?

This discussion needs to be a bit technical, and the details are given in the appendix for those who wish to understand how I did them. I will try to summarize the salient points here.

It is usually most helpful to determine what is called the whole body "effective dose" of the radiation. This dose is expressed in units called *rem*, which stands for "roentgen equivalent man". Most doses are expressed in millirems, which is 1/1000 of a rem. The dose determination is based on the results of many studies, and takes into account which organs are exposed to the radiation, as well as the nature of the radiation. If radioactive materials are ingested, the fraction of them absorbed and the time they remain in the body are also important variables to consider.

When all of the factors have been properly considered, all effective doses with the same number of millirems are supposed to have the same effects, no matter what the source of the radiation. For low doses of radiation, the major detrimental effect may be the increased

risk of cancer.¹

Tables are published which give the effective dose for most radioactive materials when ingested. The most recent tables I have seen, and the ones I used for my calculations, were published in the *Federal Register* in December, 1992. The impact of ingested radioactive material, like the impact of ingested alcohol, scales with body weight; the same amount of material will give a larger dose to a smaller person.

The Iron Studies

From data published in the paper, it seems each of the 17 youths received seven breakfasts with a minute amount of radioactive iron as a tracer, over a period of about 40 weeks. The first five breakfasts were given over a period of about 12 weeks, then there was a gap, with breakfast six given at 37 weeks and breakfast seven at 40 weeks.

Calculating the dose is complicated, because different amounts of iron were absorbed from each breakfast, and two different kinds of radioactive iron were used. Details of the calculation are to be found in the appendix. The subjects, whose ages ranged from 12 to 17 years, weighed from 70 to 135 lbs. I calculated that a 135 lb. youth received a total dose of 170 millirems. The largest dose was received by the smallest youth (70 lbs.), and I calculated that to be 330 millirems.

To understand the significance of these figures, it is helpful to know that all of us who live in Boston receive an annual dose of 300 millirems from natural sources—mostly from cosmic rays and radon in the soil. If we lived in Denver, with its 5,000 foot greater altitude, we would receive a higher background dose of 400 millirems. We all stand a 1 in 5 chance of

¹According to the National Council on Radiation Protection and Measurements (NCRP), an effective dose of 1,000 millirems poses a lifetime increased risk of cancer of 1 in 2,000. The general risk of dying from cancer is 1 in 5. The International Commission on Radiological Protection (ICRP) states that children are about three times more likely to die of cancer from a given dose than is the general population.

dying from cancer, from whatever cause. A child receiving the average dose of 230 millirems would have an additional chance of about 1 in 3,000 of dying from cancer.

The Calcium Studies

Each of the 36 participants in the oral calcium studies received two breakfasts, each breakfast containing 0.85 microcuries of ^{45}Ca (about 2 trillionths of an ounce), the radioactive isotope used. The subjects weighed from 58 to 166 lbs., and I calculate the effective doses in the appendix. The largest youth received a dose of 4 millirems, and the smallest received 12 millirems. I have also calculated the dose for the nine youths who were injected. They also received one breakfast with ^{45}Ca , and so their total dose ranged from 15 millirems (66 lbs.) to 10 millirems (98 lbs.). The adult received 12 millirems.

To put this into perspective, I can tell you that 12 millirems is the radiation dose you receive on an airplane flight from Boston to California, and back.

What Institutional Review Policies Were in Effect?

Frank Masse says that to the best of his knowledge no formal MIT review policies existed in the late 1940s and early 1950s when these studies were done. Dr. Harriet Hardy, who is now deceased, was hired to organize the MIT Environmental Medical Service in 1948. She began an informal review process and selected members of the Medical Department to review proposed studies on an *ad hoc* basis. We have found no written record to indicate that Harris' work with the Fernald School children was reviewed by MIT. Dr. Maletskos was not aware of the process that was followed to obtain approval for the involvement of the Fernald School pupils. Dr. Bronner recalls that the Fernald School was the custodian for the participants and granted permission for them to participate in the research and supervised their medical care. It was apparently customary for the physician who made possible access to the patients to assume the responsibility for securing appropriate informed consent. The 1964 Declaration of Helsinki assigned the responsibility for obtaining patient/subject consent to the physician.

The published papers in which ^{45}Ca was used as a tracer state clearly that authorization "for the use of restricted quantities of ^{45}Ca in patients institutionalized for mental inadequacy

was granted through the Subcommittee on Human Applications by the Isotope Division of the Atomic Energy Commission.” That was approval from the highest authority in the nation. A search of MIT records by Frank Masse shows that the AEC authorization was not granted to MIT, so I assume it must have been granted to the Fernald School. The beginning of the iron studies involving Fernald subjects predates the organization of the AEC, and the isotopes came from the MIT cyclotron rather than the AEC. Apparently that is why we have not found any record to indicate these studies were approved by the Atomic Energy Commission.

What Institutional Review Policies Are Now in Effect?

Although our existing committees had not yet been formed, by the early 1960s Dr. Hardy had in place a system for review of the risks posed by radioactive materials and for ensuring informed consent. One of the researchers involved in some research in which isotopes of radium and thorium were given to elderly people² described the process which was followed in the early 1960s.

- First of all, the Radiation Protection Office (RPO) reviewed the proposed protocols with the researchers and assessed the risks involved.
- Following RPO approval of the protocol, the informed consent process began. First Dr. Hardy scrutinized the protocol carefully.
 - Next, the researchers met in an assembly with potential participants in the research, explained what was involved, what the risks were, what the purpose of the research was, and asked for volunteers to participate in the research.
 - Each volunteer then had an individual meeting with two of the researchers to have the risks and procedures explained once again.

²These studies were mentioned in the 1986 Staff Report of Representative Markey’s Subcommittee on Energy Conservation and Power

- Each volunteer then had an individual meeting with Dr. Hardy.
- All volunteers were then given a three day "cooling off" period, during which they were encouraged to consult their personal physician, before signing a consent form.

In 1964, the World Medical Association adopted the Declaration of Helsinki, a code of ethics in human experimentation. In 1966 the National Institutes of Health required that all research it funded be reviewed according to the standards of the Declaration of Helsinki. I have attached a statement of the ethical requirements of the ICRP for research involving radiation, which are based on the Helsinki Declaration. They are essentially the standards which MIT has followed for more than 20 years.

Current MIT policies require the review of at least two committees, the Committee on Use of Human Experimental Subjects (COUHES) and the Committee on Radiation Exposure to Human Subjects (CORETHS). COUHES addresses the issue of the suitability of the subjects and the informed consent process, even when not required by any Federal or State agency, while CORETHS addresses the radiation risk involved. COUHES was formed in response to the NIH regulations adopted in 1966.

Before 1973, and going back to the mid 1960s, MIT had a broad license for non-human use of radioactive materials; any human use was covered under amendments to MIT's license on a case-by-case basis. In 1973 MIT obtained a broad scope NRC license for human use of radioactive isotopes and CORETHS was formed at that time.

Who Were the Subjects?

So far, we have found nothing in the MIT archives that identifies the participants. We have not yet been able to contact any surviving relatives of Professor Harris to see if they might have received and kept any useful documents. Dr. Maletskos is searching his records to see if he can find anything useful. Felix Bronner's thesis identifies the subjects in the ^{45}Ca studies only by number, but he also gives the weight and date of birth for each; when cross checked with the School records that may be enough to identify them. Dr. Bronner says he does not know of any other way to identify the participants in his research.

What Are We Doing Now?

We are taking a close look at other research conducted by MIT faculty, staff, and students during the 1940s, 1950s, and early 1960s which involved exposing humans to radiation. Whatever we learn will be freely shared. (Except for any information which might violate patient confidentiality. That information will be provided only to the appropriate institution.)

We intend to use these recent events as an occasion to verify that our oversight committees, COUHES and CORETHS, are indeed fulfilling their proper role.

Appendix

Where was the research published?

The research was published in the following four scientific papers:

- **The Iron Work**

- I. L.M. Sharpe, W.C. Peacock, R. Cooke, and R.S. Harris, *J. Nutrition* **41**, 433-446 (1950)

- **The Calcium Work**

- II. F. Bronner, R.S. Harris, C.J. Maletskos, and C.E. Benda, "Studies in calcium metabolism. Effect of food phytates on Calcium⁴⁵ uptake in children on low calcium breakfasts.", *J. Nutrition* **54**, 523-542 (1954)
- III. F. Bronner, R.S. Harris, C.J. Maletskos, and C.E. Benda, "Studies in calcium metabolism. Effect of food phytates on Calcium⁴⁵ uptake in children on moderate calcium breakfasts.", *J. Nutrition* **59**, 393-406 (1956)
- IV. F. Bronner, R.S. Harris, C.J. Maletskos, and C.E. Benda, "Studies in calcium metabolism. The fate of intravenously injected radiocalcium in human beings", *J. Clin. Invest* **35**, 78-88 (1956)

What was the Research About?

The purpose of the research was to understand how the body obtained the minerals iron and calcium from dietary sources and to find out whether compounds in cereals affected their absorption. It had been known from nutritional studies of bread that a class of chemical compounds, inositol hexaphosphates—commonly called phytates, could form insoluble compounds with iron to prevent its being absorbed from food. [E.M. Widdowson and R.A. McCance, "Iron exchanges of adults on white and brown bread diets", *Lancet* **1**, 588 (1942); R.A. McCance, C.N. Edgcombe, and E.M. Widdowson, "Phytic acid and iron absorption", *Lancet* **2**, 126 (1943)] Some cereals, for example rolled oats, contained phytates.

Others, for example Cream of Wheat, did not. The immediate goal of the research was to understand if either of these cereals was preferable from a nutritional point of view.

How Much Radiation Did The Subjects Get?

What we want to calculate is the “effective dose” of the radiation received by the participants in the research. The answer will be expressed in units of *rem*. The rem, “roentgen equivalent man” is a unit which is used to estimate the probability of the occurrence of cancer and genetic effects. For low doses of radiation, the currently accepted probability of a lifetime cancer risk for the population as a whole is $5 \times 10^{-4} \text{ rem}^{-1}$ for a fatal cancer (i.e., a risk of 1 in 2,000 for 1,000 millirem dose), and $1 \times 10^{-4} \text{ rem}^{-1}$ for a nonfatal cancer (a risk of 1 in 10,000 for a 1,000 millirem dose). The International Commission on Radiological Protection (ICRP) states that children are about three times more likely to die of cancer from a given dose than is the general population.

The rem doses of radiation are calculated so that rem values for different sources and kinds of radiation may be directly compared. The unit of radiation is the *rad*, which is the deposition of one erg of energy per gram of matter. One rem is the equivalent of one rad applied uniformly to the whole body. For those wishing to use Standard International units, the corresponding units are the *Gray* (100 rad), and the *Sievert* (100 rem). In order to calculate the rem effective dose of a particular exposure to radiation, a complicated weighting process is followed.

- There is a “quality factor” applied to the radiation which takes into account its biological effect. For x-rays, γ rays, and β radiation, the quality factor is 1.0. For α particles, it is 20, for protons it is typically 2.0, and for neutrons it ranges between 5.0 and 20, depending on the energy of the neutron.
- For radioactive material, one takes into account how much of the radioactive material ends up in various organs. Calcium, for example, tends to concentrate in the bones. In addition, materials ingested orally may not be entirely absorbed by the body. Then,

one must compute the number of rads each organ receives. That is all weighted by the probability that irradiation of that particular organ will result in a cancer.

- Where radioactive materials are involved, the amount of material is usually measured in *curies* (Ci). One Ci is the amount of material that gives 3.7×10^{10} radioactive disintegrations per second.

Tables are available which give the rem dose for various radioactive materials according to how the body is exposed to them. I used the tables of Part 20 "Standards for Protection Against Radiation", Title 10 from the December 31, 1992, Federal Register. The data are given in the table below. The table gives the ALI (Annual Limit of Ingestion): the amount of radioactive material which must be ingested to give a 5,000 millirem dose to a 160 lb. adult. I have also included in the table the fraction of ingested radioactive material which is assumed to be absorbed by the body. (5,000 millirems is the annual dose allowed a worker who is exposed to radiation in his or her occupation.)

ISOTOPE (Oral)	Assumed Absorption	Radioactivity Permitted	Effective Dose
^{55}Fe	10%	9,000 μCi	5,000 millirem
^{59}Fe	10%	800 μCi	5,000 millirem
^{45}Ca	60%	2,000 μCi	5,000 millirem

The permitted radioactivity scales with weight. That is, a person who weighed 80 lbs. would need to ingest only 1,000 μCi of ^{45}Ca to get a dose of 5,000 millirems.

The Iron Studies

From data in the paper, it seems each of the 17 youths (whose ages ranged from 12 to 17 years) received seven breakfasts with a small amount of radioactive iron as a tracer, over a period of about 40 weeks. The first five breakfasts were given over a period of about 12 weeks, then there was a gap, with breakfast six given at 37 weeks and breakfast seven at 40 weeks.

The radiation dose from this study can be calculated from the data in the paper in the following way. The iron isotopes were made in the MIT cyclotron and the tracer consisted of either ^{55}Fe or ^{59}Fe , as indicated by the entry for each meal in the table on the next page. The detector efficiency was different for the two isotopes (3% for ^{55}Fe emitting x-rays, 25% for ^{59}Fe emitting β particles) and so I get a different number for each when converting from the data in the paper, in detector counts per minute (c.p.m), to radioactivity, in disintegrations per minute (d.p.m.). Then the radioactivity is converted to curies (1 Ci = 3.7×10^{10} disintegrations per second). Since the absorbed iron was actually measured, and differed in some cases from the 10% assumed in the standard tables, we should use the actual values. The last step is to use the absorption data from the paper to calculate the radioactivity absorbed and then to convert that to millirems. From the table above, I calculate that for a person weighing 100 lbs. the dose for 1.0 μCi , if the ^{55}Fe is 100% absorbed, is:

$$^{55}\text{Fe} : \frac{5000}{9000} \times \frac{160}{100} \times \frac{10}{1} = 8.9 \text{ millirem}$$

While for ^{59}Fe , I get:

$$^{59}\text{Fe} : \frac{5000}{800} \times \frac{160}{100} \times \frac{10}{1} = 100 \text{ millirem}$$

The weights of the subjects varied from about 70 to 135 lbs., so I calculated the dose for both of these weights, as well as the mean weight of 100 lbs. The dose calculations show that the maximum dose the smallest youth would have received was 330 millirems of radiation above the natural background (300 millirems per year). The average would have received 230 millirems, and the largest got 170 millirems. The results are given in the table below.

Quantity \ Breakfast No.	I	II	III	IV	V	VI	VII	Total
Detector (10^6 c.p.m.)	2.0	1.2	2.0	2.0	2.0	3.0	1.3	
^{55}Fe activity (10^6 d.p.m.)	66		66		66	99		300
^{59}Fe activity (10^6 d.p.m.)		4.8		8.0			5.2	18
Activity, (μCi)	30	2.2	30	3.6	30	45	2.8	
Percent Fe absorbed	4.43	17.4	1.74	9.81	26.9	5.76	8.84	
Activity absorbed, (μCi)	1.33	0.38	0.52	0.35	8.07	2.59	0.25	
Effective dose, mrem (70 lb.)	17	54	6.6	74	103	33	36	324
Effective dose, mrem (100 lb.)	12	38	4.6	52	72	23	25	227
Effective dose, mrem (135 lb.)	9	28	3.4	39	53	17	19	168

It would seem that the corresponding lifetime risk of a fatal cancer could be calculated by multiplying the total dose (in millirem) by 5×10^{-7} , so that a 100 lb. subject would have a lifetime risk of 1.1×10^{-4} of contracting a fatal cancer. However, it is suggested by the ICRP that children suffer from two to three times the detriment that adults do from radiation exposure. Thus we might expect $17 \times 3 \times 1.1 \times 10^{-4} = 0.006$ extra cancers in the group of 17 youths who participated in the study. To be more conservative, we might consider the smallest youth, who received an effective dose of 330 millirems. (The natural background radiation in Boston is 300 millirems per year, and in Denver it is 400 millirems per year.) Thus, I would calculate for the most vulnerable subject, the youth who weighed 70 lbs., an increased lifetime fatal cancer risk of 5×10^{-4} or 1 in 2,000 as a result of his participation in the study. Note that the normal lifetime risk for someone to contract cancer is 1 in 3, and the normal lifetime fatal cancer risk is 1 in 5.

The Calcium Studies

These are described in the papers numbered "II" through "IV", above. These calculations are easier to do. First, the absorption of the calcium was found to be about 60% in the two studies where ^{45}Ca was given orally, so we may use the data from the first table above. Each participant received two breakfasts, each with $0.85\ \mu\text{Ci}$ of ^{45}Ca . For the third study, paper "IV", a single injection of calcium was given nine youths ($0.75\ \mu\text{Ci}$) and one adult ($2.02\ \mu\text{Ci}$); we should assume this is 100% absorbed. From the thesis of Felix Bronner, I learned that the nine youths who received the injections also were given, on another occasion, a single breakfast containing $0.85\ \mu\text{Ci}$ of ^{45}Ca . I included that in the dose shown for paper IV in the table below. From these data, and the weights of the participants from the paper, I calculate the following effective doses, for the smallest and largest participants in each study.

STUDY	Radioactivity Given (^{45}Ca)	Weight of Smallest	Dose of Smallest	Weight of Largest	Dose of Largest
Paper II	$1.7\ \mu\text{Ci}$	80 lbs.	8.5 millirem	166 lbs.	4.1 millirem
Paper III	$1.7\ \mu\text{Ci}$	58 lbs.	11.7 millirem	122 lbs.	5.6 millirem
Paper IV	$0.75\ \mu\text{Ci}$	66 lbs.	14.9 millirem	98 lbs.	9.8 millirem

The adult in paper 4 weighed 113 lbs. and received a dose of

$$\frac{2.02}{2000} \times \frac{160}{113} \times \frac{1}{0.6} \times 5000 = 12 \text{ millirem}$$

A passenger on a round trip airplane flight from Boston to California receives an extra dose of 12 millirems. For a child this imposes an increased risk of a fatal cancer of 1.8×10^{-5} or 1 in 55,000. Recall that the normal lifetime risk for someone to contract cancer is 1 in 3, and the normal lifetime fatal cancer risk is 1 in 5.

How Much Radioactive Material Was Given?

Several people have asked how much radioactive iron or calcium was given to the subjects. A μCi is a very small amount of material, as I shall now calculate. The amount of material in a curie can be calculated from the half life. For $1\ \mu\text{Ci}$, the number of grams is

$$\frac{A}{6.023 \times 10^{23}} \times \frac{3.7 \times 10^4}{0.693} \times T_{1/2}$$

where A is the gram atomic weight and $T_{1/2}$ is the half life, in seconds. The results are:

ISOTOPE:	⁵⁵ Fe	⁵⁹ Fe	⁴⁵ Ca
$T_{1/2}$, seconds:	1.3×10^8	3.8×10^6	1.4×10^7
Atoms per μ Ci:	6.7×10^{12}	2.0×10^{11}	7.5×10^{11}
Grams per μ Ci:	6.2×10^{-10}	2.0×10^{-11}	5.6×10^{-11}

A gram is about 1/28 of an ounce. The typical amounts of ⁵⁵Fe in a breakfast were about 30 μ Ci, or 1/1,500,000,000 ounce; ⁵⁹Fe amounts were about 3 μ Ci, or 1/500,000,000,000 ounce. The ⁴⁵Ca amounts were all about 1 μ Ci, or 1/500,000,000,000 ounce of radioactive calcium.

Who Sponsored This Research?

The research using radioactive iron was supported entirely by the Quaker Oats Company. The published articles using ⁴⁵Ca acknowledge sponsorship from the Quaker Oats Company, the National Institutes of Health (NIH Contract A-81 and A-81[C]), and the Atomic Energy Commission (AEC Contract AT[30-1]952). The Quaker Oats and NIH contracts were to the Nutrition Department, while the AEC contract supported the Radioactivity Center, part of the MIT Laboratory for Nuclear Science.



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March 5, 1994

MEMO TO: The Task Force to Review Human Subject Research
Massachusetts Department of Mental Retardation

FROM: Dr. Roy Shore, Professor of Environmental Medicine *RES*

SUBJECT: Review of the MIT-Fernald School Nutrition Research Involving
Radioactive Tracers and Human Subjects

General Comments

From the perspective of epidemiology and risk assessment, the report that I was sent for review was sound and prudent in its risk assessment. The risk assessment method was in accordance with the approach and numerical estimates of the National Council on Radiation Protection and of international bodies as well (International Commission on Radiological Protection (ICRP) and the United Nations Scientific Council on the Effects of Atomic Radiation (UNSCEAR)). If the dose-estimation procedures are approximately correct (and I am not expert enough in dosimetry to judge that), then the risks are unlikely to be any greater than those stated, and may well be several times less because of the conservative, "worst case" assumptions used in the dose estimation.

As the report points out, the doses incurred by these children are of a similar magnitude as variations in doses to people that occur by virtue of living in different geographic locations, flying in airplanes, having diagnostic medical or dental x rays, etc. Hence, the risks were commensurate with many others that we accept, and far less than some voluntary risks such as those of smoking. All in all, the risk from the small exposures at the Fernald School are minor. It seems to me that the principal remaining issue is the bioethical one: whether there was adequate informed consent.

Specific Comments

On p. 3 of Dr. Litster's January 2 memo and p. 5 of the Jan. 13 memo, allusion is made to the natural background dose of 300 millirem per year. I find this terminology questionable and confusing, in that this is not actually a dose typically received by any organ of the body. Residential radon gives the lungs a very large dose (up to several rem) and the rest of the body typically receives only 80-100 millirem per year. When risk-related weights for different organs are applied according to a scheme of the ICRP, it produces an average risk for background radiation which is numerically equivalent to what would obtain if the entire body had in fact received 300 millirem. But

that is a different matter than saying that the body actually receives 300 millirem per year of background radiation.

It is noteworthy that the dose estimates were made high by assuming that 100% of the iron isotopes was absorbed by the body (p. 13), when the data-derived average was about 10%. This is therefore a conservative approach, but in view of the variation among individuals in absorption and retention it is better to err on the side of prudence.

The Task Force might want to consider making a separate risk calculation regarding leukemia, since, should a leukemia occur among these boys, there is a greater probability that it might be due to the radiation received than there is for other types of cancer.

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24 February 1994

Rev. Doe West
Project Coordinator
Task Force to Review Human Subject Research
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Dear Rev. West,

Thank you for your letter of 17 February 1994, and the accompanying material. I have read the Internal Memorandum of Dr. David Litster dated 2 January 1994 and the transcript of his testimony dated 13 January 1994. I have glanced through the scientific reports which you also sent, but they are outside my area of expertise and I cannot claim to understand them.

Let me first outline the background that may have led Dean Adelstein to suggest me as an outside reviewer of this matter. I am neither radiobiologist nor nutritionist. My work has been in epidemiology, specifically the epidemiology of cancer and of congenital malformations. I have conducted some original research on radiation effects in humans, particularly on the role of diagnostic x-rays on cancer risk in the fetus and on the long-term effects of radiotherapy for carcinoma of the cervix. I have served on a number of committees dealing with radiation matters - the NAS Committee on the Biologic Effects of Ionizing Radiation (BEIR I), the NAS Advisory Committee to the Federal Radiation Council, several other NAS ad hoc committees dealing with specific issues, an Expert Panel of the World Health Organization, the Science Advisory Committee of the Radiation Effects Research Foundation (which I chaired for one year), and the American College of Radiology Committee on Radiation Exposure of Women - but I have served on these committees as an epidemiologist, not as an expert on radiation. What little I know of the substance of the matters before the Task Force has rubbed off on me in the course of participation in these committees and councils. Perhaps relevant, also, is an experience of 40 years of research using human subjects (although not experimentally) both before and after the marked change in attitudes towards and requirements for such research that took place in the late 1960s.

With respect to your first question, Dr. Litster's report seems to me straight forward and accurate. I am not in a position to question the exposure levels estimated by Mr Harris, but given his expertise I think they are likely to be as accurate as can be achieved, and they are in a range that does not surprise me. I

agree with Dr. Litster's conclusions that the informed consent procedure used in these studies "would not pass muster today" (page 7) and that such studies would probably not be permitted today "even with the low radiation doses that were used and informed consent of parents or guardian (had been obtained)." (page 8) On the other hand there are a great many things that went on both in clinical practice and in research laboratories in general in those days that would not pass muster today. There were different expectations of investigators then, and even if an investigator had sought external review of his proposal the mechanisms were not in place to undertake it.

With respect to your question about how the information should be phrased in a report to the medical care team, it should be noted, perhaps, that the cancer risks estimated by NCRP and ICRP for low-level exposures to radiation are speculative. They are based on extrapolation using mathematical models of curves derived from observations of the effects of radiation exposures many times higher than those that any of the subjects of these experiments received. The shape of the exposure-response curve at levels below, say, 50,000 mrem are quite controversial. The lowest radiation levels at which effects are thought by some to be observed are those associated with prenatal diagnostic x-rays, and here the causal nature of the exposure, as well as the levels of exposure, are subjects of debate. Of course, leukemia or some other cancer may occur by chance in some of these subjects (we can expect it in about a quarter of them eventually, as in any group of children), but it is inconceivable to me that any increased risk of leukemia or other cancer will be demonstrable among them. I know of no disease, sign or symptom that persons caring for these children should be on the lookout for. I have not seen recent data on radiation exposure in the general population, but I suspect that a large majority of Americans have received as much or more radiation from one source or another as did the children in these experiments.

As for the offspring of these subjects, extensive studies of the children of Japanese A-bomb survivors, who received exposures many orders of magnitude larger than these study subjects, have revealed no evidence of genetic damage.

It is gracious of you to offer an honorarium for this review, but it is not necessary. I hope I have been of service. You may make such use of this letter as you wish.

Sincerely,



Brian MacMahon, M.D., Ph.D.

Henry Pickering Walcott Professor of Epidemiology, Emeritus
Harvard School of Public Health

REPORT TO THE TASK FORCE

BY

JOSEPH L. LYON, M.D., M.P.H.

This report summarizes my observations and recommendations during my visit with the Task Force members at the Fernald School, Thursday, April 7, 1994.

The release to the public of a large number of documents concerning human experiments involving radioactive materials by the Secretary of the U.S. Department of Energy on December 26, 1993, prompted the creation of this task force. The four experiments that prompted the creation of this task force were conducted at the Fernald and Wrentham Schools between 1943-1973. Two experiments at Fernald examined the absorption by the human body of radioactive calcium and iron in the presence of other dietary chemicals which were believed to block their absorption. An additional study at Fernald School used iodine-131 to determine if Down's Syndrome (a genetic defect referred to as trisomy 18 because of an extra chromosome on chromosome 18) impaired the functioning of the thyroid gland. The fourth study was conducted at the Wrentham School to determine the dose of iodine necessary to stop the thyroid gland from absorbing iodine from the blood. Its purpose was to provide information on the amount of iodine that would have to be given in the event of an accidental contamination of a large area by radioactive iodine.

SUMMARY OF MY COMMENTS AT THE TASK FORCE MEETING:

General Comments

The work done by the committee staff to locate the records of these studies and identify possible participants is commendable. The level of record keeping for such events is not unusual for studies of this time period, though the failure to find documentation in the records held by the two schools is a concern.

Retention of records by a researcher that contain personal medical information is problematic. Both paper and electronically stored records have come into the possession of other researchers, e.g., graduate students, and this can create serious problems for everyone. Because of this problem the State of Utah created a legal entity to store such records. I will forward copies of this legislation to you in the next few days.

Children exposed to ionizing radiation generally manifest the excess risk of leukemia in the first 15 years after the exposure. The risk of excess leukemia for these two groups is extremely low and would be impossible to detect in any kind of an epidemiologic study.

The two studies of absorption of radioactive iodine by the thyroid gland are of greater concern because the amount of radiation exposure was much larger than from the tracer studies. The study of greatest concern was the one done at the Fernald School on children with Down's Syndrome. The radiation exposure was about ten times greater than in the study done at the Wrentham School. The risk from the increased radiation exposure was likely lessened by the known short life expectancy of children with Down's Syndrome. Thyroid cancers in men occur mostly after age 45. This is not the case for women where about half the expected cases occur between ages 20-40. The other group involved were the five parents of Down's Syndrome children who also received radioactive iodine. They would have a normal life expectancy.

The children who received radioactive iodine at the Wrentham School were younger in age than the children at the Fernald School, and the greater sensitivity of their thyroid gland to radiation needs to be considered. I will develop estimates of risk of both groups, but this task will not be finished for several weeks.



HARVARD MEDICAL SCHOOL DEPARTMENT OF RADIOLOGY
JOINT PROGRAM IN NUCLEAR MEDICINE
BETH ISRAEL HOSPITAL • BRIGHAM & WOMEN'S HOSPITAL •
DANA-FARBER CANCER INSTITUTE • THE CHILDREN'S HOSPITAL

24 March 1994

Doe West
Project Coordinator
Task Force on Human Subject Experimentation
Department of Mental Retardation
Commonwealth of Massachusetts
PO Box 9108
Belmont, MA 02178-9108

Dear Reverend West,

You have asked me to review the report of J. David Litster and the critiques of Brian MacMahon and Roy Shore on the radiation doses and possible consequent risks to the former students at the Fernald School who were administered radio-iron and radio-calcium tracers in the 1940's and 1950's. In this letter, I will also try to convey something about how these risks are estimated and a quantitative estimate of their magnitude.

We know that exposure to high doses of radiation (hundreds of rem*) leads to two kinds of biological effects in humans and animals. The early effects include bone marrow depression with consequent infection and bleeding when the whole body is irradiated, and specific tissue and organ diseases such as cataracts of the eye when parts of the body are irradiated. These effects have a threshold of dose below which they are not seen. This threshold is much higher than the doses to which the former students were exposed and thus we need not be concerned about them. Moreover, such effects appear shortly after exposure and, in some instances such as bone marrow depression, are repaired with time.

The late effects fall into two categories: an increase in the incidence of cancers and an increase in hereditary defects. Hereditary defects have not been observed in humans, but we know that exposure of fruit-flies and mice to high and moderate doses of radiation produces inheritable changes and that their frequency increases with increasing dose and decreases with lowering dose-rate. Extrapolating from mice to humans, it has been estimated that the hereditary effects of radiation are about

* Although the international community employs sieverts/Sv (=100 rem) as the unit of absorbed radiation, I will use rem (=1000 mrem or millirem) in this letter as these are the units used by Professor Litster.

1/10th that of the cancer producing effects and probably less".

The late-appearance of cancers has been seen in humans as all are aware. Radium-dial painters, who licked their brushes, developed bone cancers; early radiologists who fluoroscoped with unshielded sources and feeble screens developed cancer on their fingers; patients who received high radiation doses to their spines to treat arthritis developed leukemia from the irradiated bone marrow included in the field of irradiation.

The largest group of individuals exposed to a range of radiations are survivors of the atomic bombings of Hiroshima and Nagasaki in 1945. This group has been the subject of intensive study for the past forty-five years. The earliest cancers to appear were the leukemias but subsequently excess cancers were found at other sites including stomach, lung, breast, urinary tract and others. In 76,000 survivors, 5,936 cancers had appeared by 1985 of which 344 were in excess of those expected. It is from this group that the risks of developing cancer have been derived.

The most comprehensive estimates of radiation risk from the atom-bomb survivors were performed by the U.S. National Research Council (NRC) in 1990 (BEIR V) and the United Nations Scientific Committee on the Effects of Atomic Radiation in 1988 (UNSCEAR). In extrapolating to low doses, the committees had to make some assumptions. Perhaps the most important was that effects were proportionate to dose even at the lowest levels and that there is no threshold below which cancers cannot be induced.

In addition to trying to estimate the late effects of low-level radiation effects by extrapolation from high and moderate dose exposures, attempts have been made to do this directly from populations exposed to low levels such as individuals living in high background areas and those occupationally exposed. Because the numbers are small the results are generally statistically unreliable with some proponents claiming that they show the extrapolated risk-estimates either to be too high or too low. In my view, the prudent course is to accept the NRC and UNSCEAR recommendations.

For this reason, I have used the NRC and UNSCEAR recommendations in estimating the medical risks for those to whom radio-iron and radio-calcium were administered. The method is that of the International Commission on Radiation Protection (ICRP) and the National Council on Radiation Protection and Measurements (NCRP). They employ a quantity called an "effective dose", that is the

" Because hereditary effects have not been observed in humans they can only be estimated from animal experiments. However, they have been looked for carefully in the offspring of atom-bomb survivors without result and, thus, the sense is that humans are no more sensitive to these effects than mice, perhaps less.

absorbed dose to the several organs making up the body corrected for the relative radiation sensitivity of the various tissues.

At low doses and dose-rates the NCRP proposes a risk factor of 5 cancers in 10,000 individuals per rem (1000 mrem) exposure. Based on this risk factor I estimate the additional cancer risk (i.e. that over the normal expectation) to be:

3 in 10,000 for those administered radio-iron;
less than 1 in 100,000 for those administered radio-calcium.

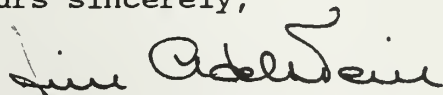
For comparison purposes, I provide the following:

1. The lifetime risk of developing cancer is 22% or 22 in 100, 2,200 in 10,000 or 22,000 in 100,000. In the United States, taken by state this varies from 16 to 25%, a variation considerably greater than the excess risks calculated for the students.
2. The lifetime risk of dying from electrocution is about 4 in 10,000. The lifetime risk of being struck by lightning is about 4 in 100,000 (assuming 70 years of life).
3. The absorbed radiation dose from the radio-calcium study was about that for a skull or spine x-ray, for the radio-iron study about that for a colon (barium enema) x-ray or brain scan.

Given these estimates, I am in agreement with Drs. Litster, MacMahon and Shore.

I hope this helps.

Yours sincerely,



S. James Adelstein, MD, PhD
Paul C. Cabot Professor
of Medical Biophysics

P.S. The following brief bibliography contains most of the material:

Radiation Dose to Patients from Radiopharmaceuticals. Addendum 1 to ICRP Publication 53, Pergamon Press, Oxford 1994.

Risk Estimates for Radiation Protection. NCRP Report No. 115, Bethesda 1993.

Cancer Statistics. CA Vol. 44, No. 1, pages 7-26, 1994 (A journal of the American Cancer Society).

The Nuremberg Code

1. The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated so as to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.

The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.

3. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.

4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.

5. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.

6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.

7. Proper preparation should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.

8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all states of the experiment of those who conduct or engage in the experiment.

9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.

10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

U.S. v. Brandt, in 2 Trials of War Criminals Before Nuremberg Military Tribunals (Oct. 1946-Apr. 1949) 181-84 (1950), quoted in 24 Syracuse Law Rev. 1067 (1973).

The Declaration of Helsinki

It is the mission of the doctor to safeguard the health of the people. His knowledge and conscience are dedicated to the fulfillment of this mission.

The Declaration of Geneva of The World Medical Association binds the doctor with the words: "The health of my patient will be my first consideration" and the International Code of Medical Ethics which declares that "Any act or advice which could weaken physical or mental resistance of a human being may be used only in his interest."

Because it is essential that the results of laboratory experiments be applied to human beings to further scientific knowledge and to help suffering humanity, The World Medical Association has prepared the following recommendations as a guide to each doctor in clinical research. It must be stressed that the standards as drafted are only a guide to physicians all over the world. Doctors are not relieved from criminal, civil and ethical responsibilities under the laws of their own countries.

In the files of clinical research a fundamental distinction must be recognized between clinical research in which the aim is essentially therapeutic for a patient, and the clinical research, the essential object of which is purely scientific and without therapeutic value to the person subjected to the research.

I. BASIC PRINCIPLES

1. Clinical research must conform to the moral and scientific principles that justify medical research and should be based on laboratory and animal experiments or other scientifically established facts.

2. Clinical research should be conducted only by scientifically qualified persons and under the supervision of a qualified medical man.

3. Clinical research cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.

4. Every clinical research project should be preceded by careful assessment of inherent risks in comparison to foreseeable benefits to the subject or to others.

5. Special caution should be exercised by the doctor in performing clinical research in which the personality of the subject is liable to be altered by drugs or experimental procedure.

II. CLINICAL RESEARCH COMBINED WITH PROFESSIONAL CARE

1. In the treatment of the sick person, the doctor must be free to use a new therapeutic measure, if in his judgment it offers hope of saving life, reestablishing health, or alleviating suffering.

If at all possible, consistent with patient psychology, the doctor should obtain the patient's freely given consent after the patient has been given a full explanation. In case of legal incapacity, counsel should also be procured from the legal guardian; in case of physical incapacity the permission of the legal guardian replaces that of the patient.

2. The doctor can combine clinical research with professional care, the objective being the acquisition of new medical knowledge, only to the

extent that clinical research is justified by its therapeutic value of the patient.

III. NON-THERAPEUTIC CLINICAL RESEARCH

1. In the purely scientific application of clinical research carried out on a human being, it is the duty of the doctor to remain the protector of the life and health of that person on whom clinical research is being carried out.

2. The nature, the purpose and the risk of clinical research must be explained to the subject by the doctor.

3a. Clinical research on a human being cannot be undertaken without his free consent after he has been informed; if he is legally incompetent, the consent of the legal guardian should be procured.

3b. The subject of clinical research should be in such a mental, physical and legal state as to be able to exercise fully his power of choice.

3c. Consent should, as a rule, be obtained in writing. However, the responsibility for clinical research always remains with the research worker; it never falls on the subject even after consent is obtained.

4a. The investigator must respect the right of each individual to safeguard his personal integrity, especially if the subject is in a dependent relationship to the investigator.

4b. At any time during the course of clinical research the subject or his guardian should be free to withdraw permission for research to be continued.

The investigator or the investigating team should discontinue the research if in his or their judgment, it may, if continued, be harmful to the individual.

HOUSE No. 4609

The Commonwealth of Massachusetts



THE COMMONWEALTH OF MASSACHUSETTS

EXECUTIVE DEPARTMENT

STATE HOUSE • BOSTON 02133

(617) 727 3600

WILLIAM F. WELD
GOVERNOR

AR GEO PAUL CELLUCCI
LIEUTENANT GOVERNOR

February 24, 1994

To The Honorable Senate and House of Representatives:

We are filing for your consideration the attached legislative proposal entitled, "An Act to Require the Informed Consent of Human Subjects as a condition of Performing Research Involving the Commonwealth's Facilities, Services, or Funds." This legislation will ensure that no research or experimentation involving human subjects that relies on funding, services, or facilities of the Commonwealth, is conducted without the informed consent of the subjects involved. It is intended to prevent any repetition of undisclosed and unwanted experimentation on the disadvantaged, as has been publicly reported.

Although agencies of the Commonwealth ordinarily require informed consent before authorizing research, and many agencies have promulgated detailed regulations of this kind, this legislation ensures that informed consent will be obtained in all circumstances and establishes uniform standards of informed consent. Among other things, it requires research investigators to explain clearly to subjects the purposes of the proposed research, the procedures involved in such research, the risks the research entails, how the research results will be used, and that participation in the research is entirely voluntary. It also establishes a simple mechanism for ensuring that informed consent is properly obtained prior to the initiation of any research covered by the bill. It authorizes the promulgation and enforcement of more stringent standards governing informed consent.

We urge your favorable action on this bill.

Respectfully submitted,

William F. Weld

William F. Weld
Governor

Argeo Paul Cellucci

Argeo Paul Cellucci
Lieutenant Governor



The Commonwealth of Massachusetts

IN THE YEAR ONE THOUSAND NINE HUNDRED AND NINETY-

AN ACT TO REQUIRE THE INFORMED CONSENT OF HUMAN SUBJECTS AS A CONDITION OF PERFORMING RESEARCH INVOLVING THE COMMONWEALTH'S FACILITIES, SERVICES OR FUNDS

Be it enacted by the Senate and House of Representatives in General Court assembled, and by the authority of the same, as follows:

SECTION 1. The General Laws are hereby amended by inserting after chapter 94D the following new chapter 94E.

Section 1. No person or organization shall conduct research which involves human subjects and which uses facilities, services, or funding provided by the commonwealth or by private entities who contract with the commonwealth to provide services to individuals, without obtaining the informed consent of the subjects involved in accordance with the requirements of this section. As used in this chapter, "human subjects" is defined to be a living individual, "research" is defined to be any systematic investigation designed to develop or contribute to generalizable knowledge, and "research investigator" is defined to be any person or organization that conducts, or proposes to

conduct, research.

(a) To satisfy the requirements of this section, informed consent shall be obtained in writing on a form signed by the subject or his legally authorized representative prior to commencing any research. Such form shall contain at least the following information in language understandable to the subject or his legally authorized representative:

1) an explanation of the nature and purposes of the research;

2) a statement of the expected duration of the subject's participation;

3) a description of the procedures that will be used, including the identification of which procedures, if any, are experimental;

4) a description of any reasonably foreseeable risks or discomforts to the subject, or of any costs the subject may reasonably be expected to incur;

5) a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

6) a description of any benefits to the subject or

others which may reasonably be expected from the research;

7) a statement of the use that will be made of any records identifying the subject, and whether the subject's confidentiality will be maintained;

8) the name of a person whom the subject may contact with questions or concerns about the research;

9) a statement that participation in the research is voluntary and that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled; and

10) a statement that the subject may discontinue participation in the research and withdraw his consent at any time without penalty.

(b) An investigator shall seek a subject's consent only under circumstances that provide the subject or his legally authorized representative sufficient time to consider whether or not to participate in the proposed research project and that minimize the possibility of coercion or undue influence.

The consent form may not include any waiver of a subject's rights or any exculpatory language absolving the investigator, the sponsor, the commonwealth or its agents of

liability for negligence. Further, the form shall be signed by the research investigator or his designee, who shall attest to the accuracy of the information contained therein.

Section 2. No research investigator subject to the requirements of section 1 shall perform research involving human subjects without certifying to the head of the state agency that is providing funding, services, or access to facilities in relation to such research that he has complied fully with the requirements of section 1.

Section 3. Notwithstanding the provisions of sections 1 and 2, certification of compliance with Part 46 of Title 45 of the Code of Federal Regulations governing the protection of human research subjects shall be sufficient evidence of compliance with the requirements of section 1. Such certification shall be submitted in accordance with section 2.

Section 4. Nothing contained in this section shall nullify the requirements of state or local laws or regulations that provide more stringent protections for human subjects.

Section 5. State agencies may establish procedures for waiving or modifying informed consent requirements, provided that such waivers or modifications apply only to research which involves no personal interaction with human subjects and which

does not identify or permit the identification of the subjects involved.

Section 6. In addition to any other remedies available by law, including those contained in section 8 of chapter 94C and including any power to sue, any person or organization violating the provisions of this chapter may be enjoined in an action commenced in superior or probate court from continuing to utilize state facilities, services or funding, or from continuing to gain access to agency records or facilities, or to human subjects who are receiving state services. Further, any person or organization violating the provisions of this chapter may be fined not more than one thousand dollars for each violation. It shall be a separate violation for each human subject whose consent is not obtained in compliance with the provisions of this chapter.

FERNALD LEAGUE for RETARDED CHILDREN, INC.

The Fernald League is the family advocates' organization for the residents of the Walter E. Fernald State School located in Waltham and Templeton Development Center located in Baldwinville, Massachusetts. The Fernald League is a non-profit tax-exempt organization whose objective is to improve the quality of life for people with mental retardation at Fernald and Templeton and in the community. Founded in 1952, it has about 700 members and reaches about 2400 families and legislatures throughout Massachusetts and the United States through its monthly publication, the Fernald Flicker. During the last 42 years the Fernald League has:

- * Pioneered special work with low level Fernald residents, who in the 1950's received from the state only custodial care.
- * Initiated the Class Action Suit in U.S. District Court, resulting in the approval of massive improvements at Fernald, including \$90 million of building renovations, \$2 million of furnishings and equipment, and recruitment and training of over 1,000 new positions since 1976.
- * Accelerated through the Class Action Suite the opening at Fernald of The Tufts Dental Clinic. The largest and best dental clinic in the world for treatment of the mentally retarded.
- * Maintains A Buildings Representatives Committee whose members monitor their respective buildings for the quality of life of the residents: their living conditions, the maintenance of their clothing, the quality of food served and services in the buildings. Representatives also evaluate the programs available to residents, in their training, workshops and recreational activities. They tour the buildings with the Division Directors and send monthly reports to the superintendents to share this information and discuss remedies to problems and praise successes.
- * Established volunteer programs to provide needed help at Fernald.
- * Established the first sheltered workshops, now expanded to 12+ units certified by the U.S. Department of Labor and Massachusetts Department of Labor and Industries.
- * Supported establishment of CARVE, a unique program wherein selected individuals from correctional institutions work directly with the severely retarded.

ADVOCACY NETWORK INCORPORATED

Advocacy Network is the largest, pure advocacy group in Massachusetts and perhaps in the eastern United States and possibly America. Advocacy Network has assisted the mentally retarded for more than six years, building upon three prior decades of effective service under its previous corporate name, The Belchertown Friends. Effective Advocacy is the only service they offer.

Achievements:

- * Established John Burns Legal Fund in 1992 to provide financial and legal resources to combat abuse and ensure victim rights
- * Class Action Suite Ricci vs. Greenblatt in Federal Court to benefit retarded citizens
- * Achieved the adoption of the Individual Service Plan (ISP) to ensure the contract of appropriate services
- * Provide advice, counsel and emotional support to thousands of individuals and families with direct impact on improving services with private vendors and state-run program
- * Maintains a Hot-line (413-256-1313) for anyone seeking support regarding services for persons with mental retardation
- * Helped produce three documents depicting living conditions and civil rights abuses of the retarded in Massachusetts

DEVER ASSOCIATION for the RETARDED, INC.

The Dever Association is the family advocates' organization for the residents of the Paul A. Dever State School located in Taunton, Massachusetts. The Dever Association has worked to enhance and to protect the lives of family members who reside at Dever. It has endeavored to support state and private efforts to provide a happy,

healthy environment in a modern, well-maintained facility with an experienced, professional and compassionate staff. It endorses and encourages an active program to develop skills, social involvement, recreational activities, good medical supervision and emotional support. The Dever Association encourages family involvement. They notify the superintendent of deficiencies and problems that he can rectify. The Dever Association insists that parents and guardians be included in decisions regarding the care, education and future plans for residents and resist interference in this area. It supports legislation that furthers the interest of the individuals with mental retardation and fights proposed legislation that is considered damaging to the individuals with mental retardation. The Dever Association was one of the plaintiffs who were forced to bring suit in Federal Court against the Commonwealth on behalf of the residents at the Dever State School.

HOGAN/BERRY ASSOCIATION of ADVOCATES for RETARDED PERSONS, INC.

Hogan/Berry Association of Advocates for Retarded Persons was organized in 1976 as a tax-exempt organization to serve all mentally retarded persons in residence at the Hogan Regional Center, Danvers and at its Berry Campus in North Reading. It also serves the residents of the various state operated homes which exist or may become operational as community living homes in the future. Hogan/Berry Association supports a continuum of life-long services for each mentally retarded person as their individual needs dictate. This Association supports and promotes the general welfare of all mentally retarded persons of all ages living at home, in community based homes, and facilities. They are deeply concerned for and advocate on behalf of the great number of unserved and underserved persons with mental retardation in Massachusetts.

PARENTS and FRIENDS of MONSON DEVELOPMENTAL CENTER

Formed in 1969, Parents and Friends of Monson Developmental Center represents the needs and concerns of the residents at Monson Developmental Center located in Palmer, Massachusetts. They filed their class action suit in 1975 against the Commonwealth of Massachusetts to improve the living conditions and staffing. Through COFAR and VOR, Parents and Friends of Monson advocate on the state and federal levels. The Parents and Friends of Monson Developmental Center are guardians for 65 residents at Monson and the community. They look over the ward's personal and medical well being, as they would their own child. At one time they were guardians for 105 individuals. The Parents and Friends are on the New Hope Activities Committee, which employs approximately two hundred residents on and off the grounds at Monson. The workshop does contract work for various agencies and firms in the community, plus their own bottle and can redemption center. The Parents and Friends have representatives on the Monson Canteen Committee which distributes the proceeds from the Monson canteen. 75% of the proceeds are used for the residents and 25% may be used for the staff for various events.

WRENTHAM ASSOCIATION for the RETARDED

Since 1955 the Wrentham Association for the Retarded, a volunteer family group, has labored to improve conditions at the Wrentham State School and to seek an environment of dignity and hope for its residents. In December, 1975, the Association was forced to bring suit in Federal Court on behalf of the residents because inhumane, constitutionally unacceptable conditions existed at the school. Conditions over the years have improved dramatically and are continually monitored by state and federal agencies. The Federal government, through Medicaid, reimburses the Commonwealth of Massachusetts 53% of all money spent at Wrentham and the other state facilities. The Wrentham Association strongly advocates for the continuation of the state facility system. This ensures that choices are available for those retarded citizens who require the specialized care available in such a setting. The Wrentham Association works closely with state employees and their unions and urges the Commonwealth and the legislature to support the competent and conscientious people who provide a stable living environment for their family members. As a member of COFAR and VOR, the Wrentham Association advocates on the state and federal levels.

Massachusetts Coalition of Families & Advocates for the Retarded

Formed in 1982, Massachusetts Coalition of Families & Advocates for the Retarded (COFAR) to be a united

organization with clout to monitor the terms of the various Consent Decrees. COFAR is the only statewide, non-profit, non-governmental funded advocacy group made up of family volunteers. Its mission is "to promote" the general welfare of the retarded wherever they may be". COFAR believes that mentally retarded individuals should live in the residential setting most appropriate for their particular needs; whether that be the family home, a staffed apartment, a supervised community residence, or for the more severely retarded or those with other behavioral or medical needs, a large facility. COFAR members Dever Association, Fernald League, Hogan/Berry Association, Parents and Friends of Monson, Wrentham Association and the Glavin Parent association advocate on behalf of all mentally retarded people on the local, state and federal levels; with the Department of Mental Retardation, the legislature, in Congress and in the media. COFAR is the Massachusetts representative for the Voice of the Retarded.

VOICE of the RETARDED

Voice of the Retarded (VOR), founded in 1983, this national not-for-profit organization strongly favors a variety of services to meet the long-term health care needs of persons with mental retardation. VOR members in 47 states include parents and family members of mentally disabled persons, as well as providers, professionals, friends and affiliated groups. VOR is dedicated to these principles:

- * Empowerment of families
- * Choice of residential and habilitative services and supports
- * Inclusion of large facilities as part of a continuum of residential care options
- * Federal and state standards of quality assurances measurable in terms of consumer satisfaction, freedom from harm, training, programmatic continuity and quality of life.
- * Independent monitoring of all programs
- * Program design based on individual need
- * Research into causes, prevention and treatment of mental retardation
- * Continuing education of federal and state officials and the general public to the diversity of the population of persons with mental retardation

ASSOCIATION for RETARDED CITIZENS MASSACHUSETTS

Founded in 1955, Association for Retarded Citizens Massachusetts (MARC) is a voluntary, non-profit organization. The Arc was a pioneer in a number of projects and activities including:

- * Resource Parents Program - providing support to young parents whose child has a disability
- * Self-Advocacy Groups - allowing persons with mental retardation to have a role in the direction of associations activities
- * MARC Trust - insuring families and individuals plans for the long term financial needs of individuals with mental retardation

Public education and information referral were important goals of the organization. They have developed an enviable track record in the legislative and judicial arena. Some examples of achievement:

- * Passage of Chapter 766, which assures free and appropriate education to persons with special needs. This law anticipated the entitlement at the federal level.
- * Passage of Respite Care Funding and Turning 22 Law - They were the first acknowledgment that adults with mental retardation and other disabilities had the right to some type of services and a separate Department of Mental Retardation and the Early Intervention Program
- * Sponsor of the Class Action Suits against the Commonwealth of Massachusetts to defend the Constitutional rights of persons with mental retardation living in the state schools

Arc Massachusetts mission is "To promote the general welfare, protect the interests and rights of, and advocate

for the needed supports and services for individuals with mental retardation and their families; to clearly express the concerns of people with mental retardation to all citizens; to coordinate, support and augment the advocacy efforts of the member Arcs on a statewide and national basis; to provide leadership in addressing public issues and in presenting the true value of people with mental retardation in our society." Four major goals have been identified which stem from the mission:

- * Protection of individuals rights
- * Inclusion of individuals with mental retardation and their families in the community as equal participants
- * Maintenance and expansion of quality services or supports to people with mental retardation
- * Lifelong supports to people with mental retardation

In Massachusetts, there are 24 local Arcs which provide direct services to individuals and families in their communities. Although their membership and supports total 7,000, their combined strength is significantly larger given the number of families involved and supporters at local Arcs across the state. They represent the concerns and needs of 100,000 persons with mental retardation in the Commonwealth.

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10.07 cont.

- (c) The proposed research cannot be carried out without the waiver; and,
 - (d) The subject does not object, by verbal or nonverbal means, to participation in the research.
- (6) The Committee may waive the requirement of informed consent for a research project involving access to private information but only if it finds and documents that:
- (a) the research consists of the study of historical records, and to require the research investigator to obtain informed consent from large numbers of relatives or descendants would make the research impracticable to conduct; or,
 - (b) the research consists of a review of records for the sole purpose of extracting information for a demographic or statistical study in which no person can be identified.
- (7) Where a research investigator wishes to request a waiver of the requirement to obtain informed consent, he or she must submit to the Committee specific and detailed reasons for seeking such waiver as part of the research proposal submission. Before granting a waiver, the Committee may impose such conditions as it deems appropriate to safeguard the rights and welfare of the research subjects. Such conditions may include the appointment of advocates and monitors.

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10.08 Research Approval

- (1) Basic Requirements. Before any research covered by these regulations may be approved by the Research Review Committee, the research proposal must satisfy all of the requirements listed below:
- (a) selection of subjects is equitable to the extent practicable by the objectives of the research;

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- (b) risks to subjects are minimized by using procedures consistent with sound research design and which do not present unnecessary risks to the subjects;
- (c) risks to subjects are reasonable in relation to anticipated benefits to subjects and importance of the knowledge to be gained;
- (d) informed consent will be sought and documented in accordance with and to the extent required by 115 CMR 10.07;
- (e) where appropriate, the research provides for the protection of the research subject's privacy and the confidentiality of private information;
- (f) where appropriate, the research provides for the safety of subjects through monitoring procedures and corrective interventions.

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- (2) Additional Requirements. For certain types of research as described in 115 CMR 10.08(2), the research must meet additional requirements before the Research Review Committee may approve the project.

- (a) If the research involves more than a minimal risk of physical or psychological injury to subjects, then:
 - (i) the probability and magnitude of the anticipated benefit for each subject as a result of the research must equal or exceed such risk of injury; and,
 - (ii) where applicable, there is specific authorization by a court of competent jurisdiction for any subject incapable of consent to participate in such research; and,
 - (iii) the additional consent and review procedures set out in 115 CMR 10.08(3) and (4) are met.

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- (b) If the research involves the administration of a new drug to a research subject, then:
 - (i) the use of the drug must be approved for trial in human beings by the Federal Food and Drug Administration;
 - (ii) the additional consent and review procedures set out in 115 CMR 10.08 (3) and (4) are met; and,
 - (iii) the procedures and requirements of the Massachusetts Department of Public Health that are applicable to research involving new drugs are met.
- (c) For any research project which the Commissioner, in his or her discretion, determines additional safeguards are required, one or more of the following requirements must be met:
 - (i) the additional review procedure set out in 115 CMR 10.08(3); or,
 - (ii) the additional consent procedure set out in 115 CMR 10.08(4); or,
 - (iii) such other measures as the Commissioner, or his or her designee, determines appropriate to protect research subjects.
- (3) Additional Review Procedure. The Commissioner shall designate a mental retardation professional to participate as a consultant to the Research Review Committee. This professional shall take such steps as he or she determines appropriate to review and monitor the risks and benefits to the research subjects. In addition, if the mental retardation professional determines that the risk-benefit requirements are not met for a particular research subject, participation of the subject in the research shall terminate.

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- (4) Additional Consent Procedure. A witness appointed by the Research Review Committee must be present when consent is obtained for each subject, and the witness must determine that the investigator has obtained informed consent for that subject. The witness must be a person whose training and experience are sufficient for him or her to determine whether the consent of the prospective subject is informed. The Committee may appoint more than one witness for the research project.
- (5) Notification. Within ten (10) days of approving a research project, the Research Review Committee shall notify and send a copy of the research proposal and Committee minutes to the Commissioner, and where applicable, to the facility director or regional director and head of the provider with jurisdiction over the facility or program where the research activity will be conducted. **DRAFT**
- (6) Notwithstanding approval of the research by the Committee, the facility director, or the regional director or the head of the provider with jurisdiction over the site where the research is proposed to be conducted, or the Commissioner, may at any time take any of the following action with regard to the research:
 - (a) terminate the research, if he or she determines that it is too disruptive or burdensome on the programs involved or is not in the interest of the Department or the provider;
 - (b) impose additional conditions on the research;
 - (c) delay the initiation of research until further review is completed;
 - (d) suspend the research temporarily pending further investigation or other action.
- (7) A statement of the reason(s) for the action shall be furnished promptly to the investigator(s). Any action taken pursuant to paragraph (6) of 115 CMR 10.08 is final and not subject to further review, judicial or otherwise.

10.09 Expedited Review

- (1) The expedited review procedure is a review of a research proposal by the chairperson or a subgroup of the Research Review Committee. The reviewer may exercise all of the authorities of the Committee except disapproval of the research. A research activity may be disapproved only after review by the full Committee in accordance with the applicable requirements set out in these regulations.
- (2) The expedited review procedure is permitted only for research which involves no more than minimal risk and,
 - (a) only seeks access to private information; or,
 - (b) represents only minor changes to previously approved research, to be implemented during the period for which approval is authorized.

10.10 Complaint

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- (1) Any person may file a complaint with the chairperson of the Research Review Committee about a research project approved by the Committee.
- (2) Upon receipt of a complaint, the chairperson of the Committee shall notify promptly the investigator(s) of the research that a complaint has been filed. The chairperson also shall conduct a preliminary investigation and refer the complaint to the Committee for further review and action if he or she determines that such referral is warranted.
- (3) The Committee, as part of its investigation of a complaint, shall provide the complainant and the investigator(s) of the research the opportunity to present relevant information to the Committee. Within thirty (30) days of receiving the complaint, the Committee shall take such action as it determines appropriate, including, but not limited to:
 - (a) termination of the research project;
 - (b) imposition of additional conditions on the research;

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10.10 cont.

- (c) temporary suspension of the research pending further investigation or other action; or
- (d) dismissal of the complaint;
- (4) The Committee shall give prompt notification to the complainant and the investigator(s) of its action. The Committee shall keep written records of all complaints, investigation of complaints, action taken by the Committee and reasons for such action.
- (5) Any action taken by the Committee on a complaint is final and not subject to further review, judicial or otherwise.

10.11 Funding for Research.

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- (1) A research project which provides for compensation of any research participant may not be approved unless:
 - (a) the compensation is received from or passes through an organization which has agreed that all its fiscal records pertaining to such research shall be subject to audit by the Department of Mental Retardation at any time; or
 - (b) the compensation is received from the Commonwealth of Massachusetts.
- (2) This section, 115 CMR 10.11, does not apply where the compensation consists solely of funds from a grant from a federal government agency or authority.

10.12 Sanctions.

In the event of violation of the human rights of subjects, or in the event that the research is not being conducted in accordance with applicable statutes, regulations or the requirements of the Committee, the Commissioner may impose appropriate sanctions. These may include the immediate suspension or termination of the research project and taking or seeking disciplinary action against project personnel.

REGULATORY AUTHORITY

115 CMR 10.00: M.G.L. c.19B, §§ 1, 14 and 18;
M.G.L. c.123B, § 2.

INFORMED CONSENT

Article 1 of the Massachusetts Declaration of rights provides, in pertinent part: "All people are born free and equal and have certain natural, essential and unalienable rights; among which may be reckoned the right of enjoying and defending their lives and liberty; that of acquiring, possessing and protecting property; in fine, that of seeking and obtaining their safety and happiness.

The law has long recognized "that a person has a strong interest in being free from nonconsensual invasion of his bodily integrity." *Superintendent of Belchertown v. Saikewicz*, 373 Mass. 728, 739 (1977); *Thibault v. Lalumiere*, 318 Mass. 72 (1945). "In short, the law recognizes the individual interest in preserving the inviolability of his person" *Pratt v. Davis*, 118 Ill.App. 161, 166 (1905), *aff'd* 224 Ill. 300 (1906)" *Superintendent of Belchertown v. Saikewicz*, 373 Mass. at 739.

As a matter of common law, a citizen has a right to be free of harmful or offensive touching. A common law battery in any intentional touching for which consent was not given. The common law has long recognized that a minor is not capable of giving consent. *Commonwealth v. Nickerson*, 87 Mass. (5 Allen) 518 (1862). A mentally retarded minor, likewise, is incapable of giving consent to a touching. Thus, when a medical procedure is to involve a child, the longstanding rule is that the consent of a parent is required, and absent such consent, the physician may be liable for battery. A parent, or one in loco parentis, may give consent to a procedure on a child or mentally retarded person under a theory of substituted judgment. However, the test for the consent would be, and historically has been, whether the procedure was in the "best interests" of the individual.

Reported legal cases involving consent to experimentation do not exist in Massachusetts prior to the 1940s. However, the Michigan Supreme Court in 1935 recognized the two fundamental parameters of the justification of experimentation on human subjects: a balance of risk and benefit and valid consent. The case concerned therapeutic research, i.e. research likely to benefit the subject, and the court permitted research on consenting human subjects. *Fortner v. Koch*, 272 Mich. 273, 261 N.W. 762 (1935).

In the case of *Bonner v. Moran*, 125 F.2d 121 (D.C. Cir. 1941), a Federal appellate court considered the question of consent in the following context: A fifteen year old boy agreed to donate skin grafts and blood to cousin, and required a two month hospitalization during the procedures. The Circuit Court affirmed the general rule that the consent, either express or implied, of a parent is necessary for any operation on a child. The court noted, "In deference to common experience, there is general recognition of the fact that many persons by reason of their youth are incapable of intelligent decision, as the result of which public policy demands legal protection of their personal as well as their property rights. . . . Hence it is not at all surprising that, generally speaking, the rule has been considered to be that a surgeon has no legal right to operate on a child without the consent of his parents or guardian." *Id.* at 122. The court also noted that there were exceptions to the rule, for emergency, where the child is

emancipated, or where the child is so close to maturity that the surgeon could rely on his or her consent. However, in such cases, the procedures were for the benefit of the child whose consent was accepted.

The United States Supreme Court, in a case not involving medical experimentation, expressed the following standard: "Parents may be free to become martyrs themselves. But it does not follow [that] they are free, in identical circumstances, to make martyrs of their children before they have reached the age of full and legal discretion when they can make that choice for themselves." *Prince v. Massachusetts*, 321 U.S. 158, 170 (1944).

The next most significant step in the development of a legal standard for human experimentation came with a judgment in the Nazi war criminal trials. Part of the judgment included the Nuremberg Code, which set a clear standard for the legal and scientific community. With regard to the question of consent, the Code provides:

The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated so as to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.

The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

U.S. v. Brandt, in 2 Trials of War Criminals Before Nuremberg Military Tribunals (Oct. 1946-Apr. 1949) 181-84 (1950), quoted in 24 Syracuse Law Rev. 1067 (1973). The complete text of the Nuremberg Code is set forth in Appendix

Thus, by the end of the 1940s, the medical and legal worlds were, or reasonably should have been, familiar with several basic principles concerning consent and the balancing of risks and benefits. The Code also required evaluation of any human experiment for relative risk of harm to the subject; for whether it was likely to yield results fruitful for society; for whether scientifically qualified personnel would be conducting the experiment; and other factors. Any experiment on a human subject, conducted after the Nuremberg Code was published should not have been conducted without full disclosure of the parameters of the experiment, and without knowing consent of the subject.

In the 1950's, the Massachusetts courts had three opportunities (at least so far as available decisions reveal) to consider the question of consent of medical procedures. In a series of three cases involving the transplantation of

kidneys from one twin to another, the Supreme Judicial Court found, upon expert medical evidence, that the procedures would provide medical benefit to the recipient of the kidney, as well as the donor sibling, who would derive a significant psychological benefit. Each case turned on the fact that the children were of sufficient age and intelligence to appreciate the significance of the situation, and to knowingly participate in the giving of consent. Further, the children were not affected by any institutional duress which might accompany residency in a State School. *Masden v. Harrison*, No. 68651 Eq. Mass. Sup. Jud. Ct. June 12, 1957; *Huskey v. Harrison*, No. 68666 Eq., Mass. Sup. Jud. Ct., Aug. 30, 1957; *Foster v. Harrison*, No. 68674 Eq., Mass. Sup. Jud. Ct., Nov. 20, 1957.

Responding to the increase in abuses during that time, the 18th World Medical Assembly adopted the Declaration of Helsinki. The Declaration was reprinted in the New England Journal of Medicine in 1964. The Declaration expanded on the considerations expressed in the Nuremberg Code regarding the evaluation of human experimentation for risk and benefit. The Declaration also repeated the call for full informed consent of any individual to be involved in an experiment, and his or her freedom to withdraw at any time. Again, the duty to obtain consent always remained with the researcher. The text of the Declaration is set out in full in Appendix ____.

In 1965, the National Health Advisory Board resolved that any Public Health Service research activity on humans would require prior review by institutional associates to protect the rights and welfare of individuals involved, and to insure appropriateness of informed consent procedures and of risks and medical benefits. In 1966, the United States Surgeon General accepted the resolution, and promulgated Policy #129. Thereafter, all Federal funding for human research was conditioned on institutional review in accordance with the National Health Advisory Board recommendations. The full text of PPO #129, revised July 1, 1966, as issued by the U.S. Public Health Service, is set out in Appendix _____. Archival records indicate that the State Schools, as well as local research institutions, responded to this mandate, and did establish review boards.

However, the Surgeon General's policy proved to be inadequate, leading to the enactment of Federal laws, Federal regulations, as well as stricter state controls, which will be discussed in the next section.

